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Pulmonary Tuberculosis

Directed Therapy

Cancer in Relation to Life Insurance

Medical Book News Editorials
Contemporary Progress

Vol. 73 No. 10

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EDITORIALS

Puncturing the Philanthropoids

ONE of the favorite arguments just now of the philanthropoids (De Casseres' term for the folk who devote their lives to "doing good" to their fellowmen with other people's money) in behalf of compulsory sickness insurance is to the effect that such insurance is analogous to compulsory education. That it is not analogous is made clear by Professor Smillie of Cornell University [*J.A.M.A.* 128:1005 (Aug. 4) 1945]. Our compulsory educational system was not imposed on us from above by the federal government, on a nationwide base. Moreover, "It has maintained the basic feature of local autonomy and local community determination of policy. State standards have been of great value in the improvement of the system. State subsidies to less favored communities are an essential part of the plan. The federal government has been of assistance in promotion of nationwide standards of education. But the principle of local community responsibility for schools is the very keystone of the plan, whereas a federally sponsored and administered plan would be certain to fail."

The Cure of Cancer Is Purchasable

THE charge has been made, or implied, in responsible quarters, that "while atomic physics has taken vaulting strides, biology and medicine have been sleeping unconcernedly in a disordered attic." And from the same quarters come demands that the medical sciences mobilize to combat cancer, heart disease, leukemia and poliomyelitis.

But only about $10,000,000 is actually in sight. From what source shall we obtain the necessary hundreds of millions?

"Cancer," says Waldemar Kaempffert, "kills more people in two years than we lost in almost four of war." So haste must be made as regards the necessary funds. Merely setting off rhetorical bombs like the one we have quoted in our first paragraph is more destructive than constructive. The gadflies should go to work on the sources of the needed funds.

Two billion research dollars developed the atomic bomb. Into the long-term cancer program of the Sloan-Kettering Institute for Cancer Research at the New York Memorial Cancer Center will go four million dollars, with, in addition, $200,000 a year for ten years toward operating costs. This is fine as far as it goes, but it does not meet the actual need; it is not the answer to the problem.

We accept the burden of high cost for destroying life at the same time that the cure of cancer is definitely purchasable, demurring, however, at the cost of the latter.

If the ratio of these two cost items continues to change in this fashion we may never be able to purchase the cure of cancer.

Perhaps there will be appalling loss of life on both counts as time goes on. Could it be that this is what is wanted?

Political Penicillin at Washington

THERE seems at present to be a strong demand in the Congress for legislation that would give Federal aid to the low income States, through both public and private agencies, enabling such States to supply medical aid where needed. The proponents of this aid do not wish to base it on socialized medicine or on any overall compulsory plan as proposed in the Murray-Wagner-Dingell bill. The same healthy forces in the Congress are also opposed to huge Government spending as

the panacea for every ill, as we see it in the Wagner "Full Employment" bill.

All this is very heartening. The patient is showing signs of recovery. Political penicillin seems to be available now in Washington. The Government chiropractors are apparently losing caste.

Population and the Atomic Bomb

OUR views regarding population in its relation to large manpower reserves may have to be revamped. This may be one of the social consequences of the introduction of the atomic bomb. Armies of millions would be of no avail against the bomb nor would an invader armed with the bomb require great forces of men or ships or planes. The dominant nations have hitherto thought of the maintenance of future power in terms of men. This position seems now to be lacking in force. It will be interesting to hear the population and military training experts on this point.

The Physician's Reaction to War

THE thoughts of Sigerist, of Johns Hopkins University, on the socialization of medicine are no more impressive than those of any other advocate of that weird system. His thoughts on war seem to us to be undiluted wisdom. One would hardly suppose that the two themes emanated from the same mind:

War is a social disease, like poverty or crime. When it breaks out it reminds us that we are still in the initial stages, in the prehistory of civilization, not far removed from savagery. It reminds us that although we like to play with science and kill with scientific weapons, we have not yet learned to approach the basic problems of social life—production, distribution, and consumption—scientifically. If a physician believes in his work he cannot but abhor war, which is the negation of all his efforts. When war comes he of course will do his best to alleviate the sufferings that stupidity, inefficiency, and greed have brought upon his fellowmen. And he is fortunate in that he himself is not obliged to kill. We whose lifetime falls into a period of transition, when a decaying world is committing deliberate suicide, have all spent years in uniform or shall do so. But the physician has still another task, namely, to side passionately with life against death, to fight the obvious causes of war and to help in paving the way for a better world. And he should remember that open war, after all, is merely the acute form of a disease which in its chronic form is endemic in our society. Even in the most peaceful years thousands of human beings are oppressed, crushed, and starved out in a war that is not so spectacular as the formal one but just as deadly. There is a front for the physician here, too.

Galen was surgeon to the gladiators at Rome in the second century of the Christian era. Doubtless then, as now, the doctor served at the call of the State, though the high intelligence of Galen must have execrated war itself and the devious gladiatorial mode of authorizing murder apart from war. The amphitheater was only a vicarious battlefield, after all. We have to assume that the cultured physician, traditionally noncombatant, has always seen war as Sigerist characterizes it.

Why is it that mass murder in the manner of war is condoned and the murder of individuals proscribed? The principles of morality and religion obviously do not govern mankind's sensibilities and behavior in these matters as they should; there must be a controlling factor other than these. Perhaps De Quincey, in his famous essay "On Murder, Considered as One of the Fine Arts," comes closest to the answer.

Aesthetics has to do with beauty. The spectacle of war, with its mangled boys and rat-eating prisoners, is the very antithesis of beauty.

Aesthetics comprises painting, sculpture, architecture, music, poetry and, according to De Quincey, murder.

The several fine arts are the realization of beauty through their appropriate media. The province of aesthetics is to determine the nature of beauty in general and the laws governing its expression in a concrete medium. De Quincey relates murder to these considerations.

Mass murder, by methods from the atomic bomb down to the machine gun, can never be included among the fine arts. There is a military art, to be sure, but it is not a fine art. But the individualized murder quite often presents aesthetic connotations which bring it within the fine arts category—be beautifully contrived and executed, in a sense—as De Quincey showed very convincingly in his essay. Most people can adjust to war because it is devoid of aesthetic implications, to which the "common man" is usually hostile. So they are horrified by individualized murder, no matter by what finesse achieved. If war had any aesthetic implications they would be horrified by it, too.

Since the introduction of an aesthetic phase into war is inconceivable, its abolishment is seemingly impossible. The populace is, so to speak, made for war, and war too often serves admirably the ends of ambitious and unscrupulous politicians.

—Concluded on page 312

PULMONARY TUBERCULOSIS
MODERN CONCEPT AND RECENT ADVANCES IN TREATMENT

I. Ellis Rudman, M.D.
Philadelphia, Penna.

II

IN the textbooks on tuberculosis, very little space is given to the discussion of the economics and social aspects of the disease. The pronouncement by the physician that an individual has an active tuberculous lesion in his lungs sets in motion a train of events that is often hard to foresee or visualize. The continuity—the routine existence of life—is suddenly broken. Plans, hopes, aspirations have to be held in abeyance—delayed for a long time—and sometimes often entirely abandoned. Ways of life—mode of living—have to be revamped. Frequently, homes are broken up. To obtain a "cure," savings of years are dissipated and, even after the "cure" is realized, life has to be started anew. Lack of insight into a patient's circumstances—the consideration of the medical aspects of the case only—often leads to tragic consequences.

I recall the case of Mrs. M. She was a clinic case. After a diagnosis of tuberculosis was made and her case classified as a minimal tuberculous lesion, the question arose as to how to best take care of her. Since sputum was scanty and negative for tubercle bacilli, she was counseled by the clinic physician to take the "cure" at home. Her home was the average American workman's home; modest but comfortable, located in a suburb of Philadelphia. Adequate instruction was given to her as to hygiene and sanitation and the proper disposal of any expectoration that she might bring up. Frequent visits were planned for her at the clinic. All contacts were examined. However, these arrangements did not suit the clinic nurse and social service worker. More with an eye to statistics and the monthly records of sanatorium admissions, Mrs. M. was prevailed upon to seek sanatorium care. With thoroughness and ruthlessness and utter disregard for the consequences, Mrs. M's problems were solved in this fashion. 1) The children were placed in a foster home. 2) An aged father was placed in the home for the aged. 3) The furniture was stored. 4) The husband found for himself a place in a boarding house. The patient was bundled off to a State institution. When she arrived there, she was told that all that was required in her case was a prolonged period of rest. She did very well at the institution—she gained a great deal of weight. Cough disappeared, expectoration became very scanty, sputum remained negative. After six months' time, she was given a month's furlough home. In her husband's hall bedroom, she found the solace of home. The thirty days were quickly over and she returned to the sanatorium. Soon after her arrival there, she developed a cutaneous eruption. The skin lesion, together with the finding of a 4 plus Wassermann, established the diagnosis.

TUBERCULOSIS is essentially a chronic disease; slow in onset and almost symptomless in its early stages. In most instances, except for a mild cough, slight fatigue, and listlessness, the patient is hardly aware of the seriousness of his trouble. To such cases, a prolonged stay in the sanatorium is a form of incarceration. The ennui, the boredom, and the deadly routine often mitigate against any benefits that could be derived from the "rest cure." Especially is this true of the teen age group. In August, 1939, Miss S., following a severe cold, expectorated some blood. Physical examination, confirmed by x-ray, revealed a very early tuberculous infiltration in the right infraclavicular zone. At the sanatorium she was morose, sullen, and very unhappy. She often refused to eat, and at times, to avoid coercion, threw her food out of the window. After three months' sojourn at that institution, she lost eight pounds in weight. The tuberculous lesion progressed rapidly and cavitation took place. Following another severe hemorrhage, a bronchogenic spread occurred to the contralateral side. The outcome was fatal.

The restlessness, moodiness, and irritability that often attack the sanatorium

Continued from the July, 1945 issue of the MEDICAL TIMES.

patient have been a source of worry to many a resident physician. Close questioning of patients as to the cause of these phenomena elicits various answers. A disinclination on the part of many patients to discuss personal problems is readily understandable. Occasionally a married patient will be frank enough to state that interference with normal sex life prevents the obtaining of the full benefits that sanatorium regimen and care can bring about. Close questioning of a cross section of the adult tuberculous population in a well conducted private sanatorium failed to give the impression that active tuberculosis acts as a stimulant to sexual desire. It is more probable that the superalimentation and the life of indolence has a stimulating effect on the libido rather than the disease itself, and the sex urge becomes a factor only when the disease is well under control.

THE selection of a case for home or sanatorium care depends on many factors: the acuteness of the disease, the need for constant nursing care, the social and economic status of the patient, the presence of minors in the family, the character of the lesion.

The home care in this day and age does not necessarily mean only good food, rest, and fresh air. It means also hospitalization for shorter or longer periods in a sanatorium or hospital for the performance of those procedures that will hasten recovery. The ideal method we have been taught is to hospitalize every tuberculous patient and keep him in the sanatorium until a "cure" is obtained. In many instances, this may require three to five years even when collapse therapy is applied. Though theoretically sound, in practice it is often found impossible of attainment. The city of Chicago, finding its bed capacity inadequate for the number clamoring for admission to its institutions, launched a program of ambulatory pneumothorax treatment. From 1931 to 1941, 4,810 patients were treated. 1) Pneumothorax was used without hospitalization; 2) pneumothorax was used with an initial period of bed rest and made ambulatory as quickly as possible; 3) pneumothorax was employed combined with adequate bed rest. On the whole, there was very little difference at the end of this period, statistically speaking, in the evaluation of the end results as compared to those cases who were admitted and kept in the sanatorium from the beginning to the completion of a "cure." However, the statistics of the Chicago Municipal Sanatorium do not give a complete picture of the possibilities of ambulatory collapse therapy in private practice. Here we have patients who are on a somewhat higher economic level. The home surroundings are more cheerful. Food and nursing care are more adequate. Hospitalization insurance reduces the burden and expense for periods that are required in hospitals. It should also be noted that the Chicago Municipal Sanatorium statistics included the worst years of the economic depression.

IT is not even remotely suggested that the tuberculosis sanatorium, as now constituted, has outlived its usefulness. This is simply an attempt to evaluate its proper place in the scheme of things. If its original conception was the creation of a place where all positive cases could be segregated, then, with the years, its real purpose has been sidetracked. The practice of discharging from institutions the far advanced cases is hard to condone, if the purpose of the sanatorium was to prevent the spread of infection among the general population. Like the physician in private practice, the sanatorium wants to obtain results that would reflect credit on the institution, and with this in mind, the tendency has been in recent years to facilitate the admission of incipient and moderately advanced cases and to keep the far advanced cases on the waiting list. More adequate use could be made of our State and County institutions, and a greater turnover of patients would result, if the cases successfully treated by collapse therapy were discharged and after-care furnished in properly conducted clinics, or if they were turned over to the private physician properly qualified to do this type of work. Another factor that has tended to lessen the prestige of the sanatorium has been the tendency to put on bed rest for long periods all cases admitted, no matter how suitable they are for collapse therapy. The case of Robert M. will well illustrate this point. He was diagnosed as a moderately advanced case of pulmonary tuberculosis, fibrocaseous in character and limited to the right upper lobe. After a stay of nine months in a sanatorium, he left against advice. The story behind his taking French leave bears close study. Robert M. was 28 years of age when taken

ill. A clever, good-looking chap, he quickly made his mark in his chosen field—sales promotion for a dairy concern. To finance his family during his stay at the sanatorium, he sold his home. After nine months' "rest cure," his funds depleted, he returned to the city. He was then hospitalized and a successful result was obtained by means of artificial pneumothorax. Within a period of three months, he was able to resume his former occupation.

THE total disregard for the time element in tuberculosis is sometimes appalling. It is so easy to be glib and advise the patient to relax and obtain the full benefit of sanatorium care. Why it is especially in tuberculosis that methods that would shorten hospitalization are delayed is hard to understand or condone.

The "home treatment" of pulmonary tuberculosis has assumed a new connotation in the last ten years. The textbooks no longer feature specially built sleeping porches. Though the triad of good food, fresh air, and bed rest is still the bedrock of treatment, insistence is no longer made on keeping the patient out of doors in inclement weather. In the winter, a properly ventilated, comfortably warm room is insisted upon by phthisiologists. "Home treatment" now means a sojourn in the hospital or sanatorium for longer or shorter periods as the exigencies of the case demand for the institution of positive measures and the continuation of these measures at home.

The uprooting of the patient's home life, the homesickness, and the boredom that long periods of sanatorium life entail are thus eliminated.

IN perusing the literature of fifteen or twenty years ago, we find the indications for collapse therapy, especially pneumothorax, were hard and fast. It was not to be tried except in the moderately advanced or far advanced cases. The lesions had to be primarily unilateral. As a result of these restrictions, the number of cases found suitable ranged from six to ten per cent. Though the indications have now been broadened, the contraindications remain the same. Poor results are obtained when pneumothorax is attempted in 1) miliary tuberculosis; 2) in the acute pneumonic forms, especially when found in Negroes; 3) in the cases of tuberculosis complicated by emphysema; 4) in the asthmatic cases; 5) tuberculosis complicated by cardiac disease; 6) in the uncontrolled or uncontrollable cases of diabetes mellitus.

In the early days after the popularization of artificial pneumothorax, a frequent cause for the abandonment of treatment by this method was the finding that the benefits of collapse therapy were nullified by the presence of single or multiple adhesions between the visceral and parietal layers of the pleura. These adhesions frequently prevented cavity closure. Attempts to stretch these adhesions and make the pneumothorax more effective by the increase of intrapleural pressure frequently caused serous effusions and even empyema. The work of Dr. Jacobeus of Norway showed that many types of adhesions can be severed. This has greatly increased the percentage of successful results of treatment by pneumothorax. At the present time nearly 70 per cent of the tuberculous are amenable to treatment by means of collapse therapy. The indications have been broadened to include the early infiltrations as well as the moderately advanced cases. The presence of a small amount of tuberculosis in the contralateral lung is no longer considered a bar to pneumothorax treatment, for it has been found that when the disease is brought under control in the extensively damaged side, the contralateral lesion will often take care of itself. The beneficial results of pneumothorax treatment often surpass expectation. A toxic febrile patient whose body is constantly tormented by a racking cough is quickly turned into a quiet, cheerful and hopeful patient after the first few treatments. The results are brought about 1) by the mechanical rest of the lung; 2) the approximation of cavity walls in the diseased lung; 3) the elimination of pus, mucus and debris from the bronchi; 4) the separation of the pleurae, thus causing lymph stasis; 5) active hyperemia in the compressed lung tissue; 6) toxins from the diseased portion of the lung have less access to the systemic circulation; 7) the reduction of the oxygen intake to the collapsed lung impedes the growth of the tubercle bacillus; 8) the stimulation of fibrosis in the compressed lung; 9) pulmonary hemorrhage is frequently and successfully brought under control by means of artificial pneumothorax.

The rapidity with which a sputum loaded with tubercle bacilli becomes negative, sometimes in a matter of days after

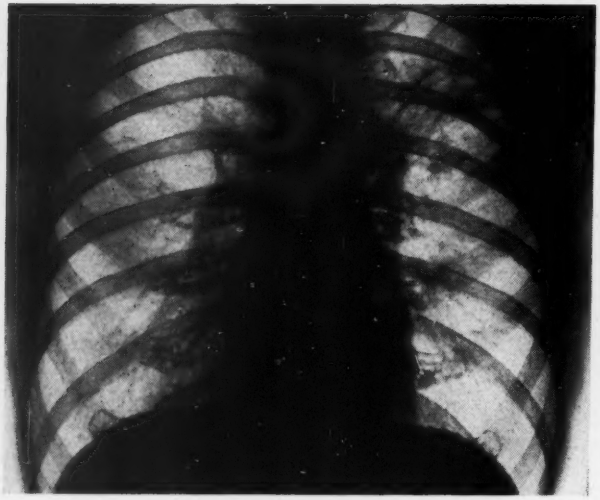


Fig. 1. Mr. W. J. S. Age 32 3/1/37 shows a fibrocaseous lesion involving the left upper lobe. Many small cavities can be seen in this area.

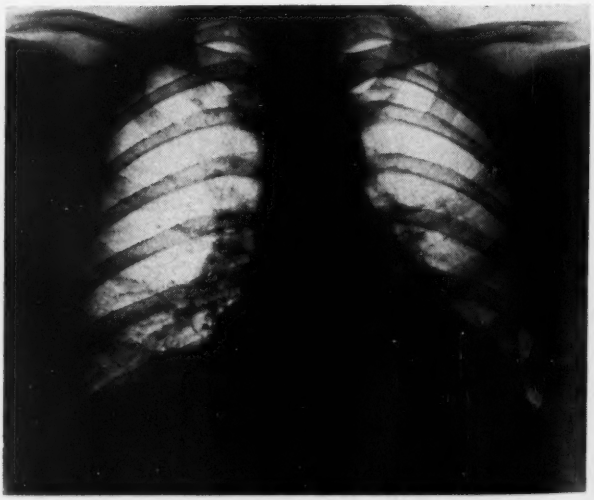
successful pneumothorax treatment, still evokes surprise in the uninitiated to this method of therapy.

IT may not be amiss at this stage of our knowledge and progress to attempt the debunking of some of the popular and accepted notions about tuberculosis. We have to reteach the public that tuberculosis is curable, that endless years in a sanatorium are not always necessary for the completion of a "cure," that the earlier the treatment is instituted the better the results, that tuberculosis is not to be considered as a contagious disease, that the spread of infection can be avoided by proper adherence to the simple rules of hygiene and sanitation.

In many institutions for the treatment of pulmonary tuberculosis, a sort of routine procedure is followed and with rare variations. First a period of prolonged bed rest. If the patient fails to show any improvement, an attempt is made to induce artificial pneumothorax. Failure of this measure to bring about the desired results is followed by another period of rest or until the air in the pleural space is completely absorbed. Then the phrenic nerve is tackled. It is either crushed, cut or removed. Lack of benefit resulting from this procedure is followed by thoracoplasty.

At this stage of our knowledge of the pathological process that takes place in the tuberculous lung and in the pleurae, such rule of thumb procedure is entirely unwarranted. From the history of the case, we can learn whether attacks of pleurisy have occurred.

Fig. 2. Mr. W. J. S. 7/8/39 shows a uniform collapse of the left lung and freedom from adhesions. The original lesion has shown evidence of absorption and retrogression. All cavities have been obliterated.



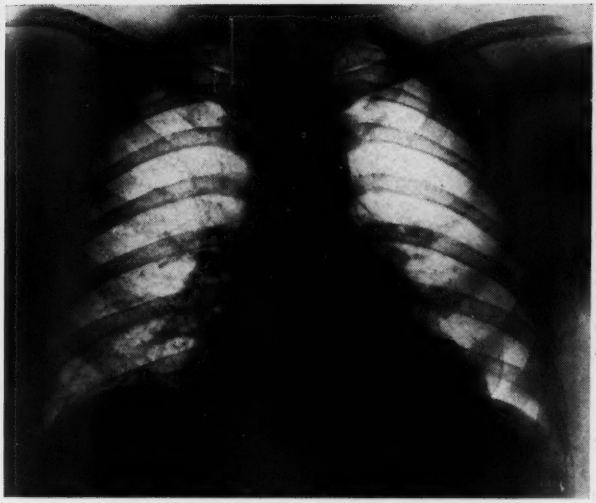


Fig. 3. Mr. W. J. S. 7/20/40. The lung has been allowed to re-expand and there remains only a small pocket of air near the left costophrenic angle. The only residual of the previous lesion in the left upper lobe is an increase in surface markings radiating from the left hilus.

The chances of finding a free pleural space after repeated attacks of pleurisy is very unlikely. Especially is it rare to be able to induce pneumothorax in a case where an effusion has occurred and the fluid allowed to absorb. Added to the information that we can obtain from the histories of the patients, the x-rays will often show unmistakable evidence of pleural thickening which will exclude any possibility of inducing pneumothorax in such cases.

ALL tuberculous disease of the lung can be grouped in two main classifications—the exudative and the proliferative. All gradations of these forms exist and supervene on each other. It is the predominance of one type of lesion or the other that decides what course is best to pursue in controlling the disease. In any given case, the deciding factor as to whether it can be treated by means of artificial pneumothorax is not the fact that the lesion is unilateral or practically so. Generally speaking, the acute exudative lesion is amenable to treatment by artificial pneumothorax if treatment is instituted early in the course of the disease. In such cases, cavitation can frequently be prevented. At times, after the collapse of the lung, caseated material that has remained in situ is expressed by the collapse of the lung and cavities, large and small, become visible. However, if the case comes to our attention after extensive cavitation has taken place, our choice of method must depend on the location of the cavitation and the character of the lesion. If the lesion has become somewhat stabilized, it may be preferable and with greater assurance of successful result to resort to thoracoplasty than to attempt to close such cavities by means of pneumothorax. It is certainly unwise to attempt pneumothorax when large cavities are located at the periphery of the lung.

The judicious use of subsequent refills after the initial pneumothorax is given must depend upon the skill and judgment of the operator. Whether a pneumothorax is to be of the hypotensive or tensive type can only be decided by the character of the lesion and the course of events. Only sufficient pressure should be employed on the sick lung to bring about reduction of temperature and amelioration of cough, and to facilitate expectoration and the gradual closure of cavitation. Care must be taken not to bring about any shifting of the mediastinal structures or to cause herniation of the lung.

THE ideal result in the ideal case is well illustrated in the accompanying x-ray films of Mr. W. J. S. On March 1, 1937, the x-ray film of Mr. S. shows a fibrocaseous lesion in the left upper lobe with multiple cavitation. After the induction of pneumothorax and in a matter of about three weeks, cough and expectoration became almost negligible, temperature returned to normal, and he gained ten pounds in weight. A film taken on July 8, 1939, shows a clearing up of the lesion, obliteration of the cavities, and only in-

—Continued on page 312

Research on Pharmacodynamics

Paulo Seabra
Fellow, National Academy of Medicine
Rio de Janeiro

A science of life indeed exists, presenting no other difficulties than its own complexity, and if the day comes—which is not to be doubted — when, thanks to much work and patience, physiology becomes definitely established as a science, then we shall be able, by means of modifications of the blood medium, to impose our will on all that world of elementary organisms which constitute our being; knowing the laws which govern their relations one to the other, we shall be able to control and vary at our own will the diverse manifestations of life.
September 1st, 1864

CLAUDE BERNARD

EXAMINING in the ultramicroscope a drop of blood in contact with a drop of colloidal quinine (hydrosol quinine base of 1 per 1000) (1) I observed that in the encountering zone of the two liquids many quinine micelles are adsorbed by the red corpuscles which then take the aspect of little crowns with many luminous points (see fig. 1).

This surprising and heretofore unknown fact (2) (3) was the starting point for the hypotheses and research work that are dealt with in this paper.

It was already known that the red corpuscles are able to adsorb crystalloids and even lyophilic colloids as certain proteins (4); however, it was generally believed that the lyophobic colloids, when introduced into the blood, are not adsorbed by the red corpuscles but by the cells of the reticuloendothelial system which becomes blocked (5) (6) (7) because of its characteristic granulopexia.

I also found that the blood reaction has a great influence upon the capacity of the red corpuscles to adsorb the colloidal quinine; the blood in acidosis shows intensive erythrocytic adsorption, while in alkalosis the adsorption is weak or even negative, that is, the colloidal micelles keep their Brownian movement without affecting the red corpuscles.

This phenomenon is easy to observe: a drop of blood is placed in a vacuum and all the CO_2 is extracted, thus producing an alkalosis which prevents the erythrocytic adsorption of the colloidal quinine. By blowing air with a pipet over the drop of blood there appears an acidosis due to the CO_2 from the exhaled air. Consequently, the adsorption is reestablished with an intensity even greater than normal; actually, all the red corpuscles are now covered with the colloid, some of them with double layers of micelles (see fig. 2). Using each of the gases separately it becomes evident that this action is due to the CO_2 and not to the O_2 though the latter is also present in the exhaled air.

Experiments with various animals demonstrated that erythrocytic adsorption is much more intensive in rabbits than it is

Lecture given at the National Academy of Medicine. Rio de Janeiro, November 30, 1944.

Table 1

Erythrocytic Adsorption
Intensity according to different natural blood pH

Samples	Blood pH (a)		Erythrocytic Adsorption of Colloidal Quinine
	Individual	Average	
Rabbit No. 1	7.20		
Rabbit No. 2	7.25	7.23	+++
Rabbit No. 3	7.26		
Man No. 1	7.23		
Man No. 2	7.23		
Man No. 3	7.23	7.24	++
Man No. 4	7.28		
Sheep No. 1	7.33		
Sheep No. 2	7.35		
Sheep No. 3	7.40	7.37	+
Sheep No. 4	7.40		

in man, whereas it is very weak in sheep. Table 1 shows the degrees of intensity revealed by these experiments:

Consequently, any acidosis producer would intensify adsorption in the sheep and any alkalosis inducer, on the other hand, would weaken it in the rabbit.

Acidosis was induced in the sheep by an intramuscular injection of 5 cc. of a 40% solution of calcium chloride. The results of one of these experiments are condensed in table 2:

Table 2

Influence of Acidosis

(5 cc. of a 40% solution of $CaCl_2$ in sheep)

Before	+
After 5 minutes	+
After 10 minutes	++
After 20 minutes	+++
After 50 minutes	++++
After 60 minutes	+++
After 70 minutes	++
After 80 minutes	(—)

Alkalosis was induced in the rabbit by injecting 5 cc. of a sodium bicarbonate solution of 10% through the peritoneal route. Results are shown in table 3:

Table 3

Erythrocytic Adsorption
Influence of Alkalosis

(5 cc. $NaHCO_3$ 10% sol. in rabbit)

Before	+++
After 2 minutes	+++
After 5 minutes	++
After 15 minutes	(—)
After 30 minutes	++++
After 60 minutes	+++

At the end of these experiments in both rabbit and sheep, there is an inversion of the phenomenon, because the violent disturbance of the acid-base balance provokes a contrary organic reaction.

The pH acts also on the erythrocytic adsorption even when the red corpuscles have been separated from the plasma and placed in an isotonic buffer of primary-secondary phosphates (*). See results in table 4:

Table 4

Erythrocytic Adsorption

Influence of the pH upon human red corpuscles

pH 5.8	++++
pH 7.0	++
pH 7.5	(—)
pH 8.0	(—)

With these experiments it is proved that the acid-base balance or the CO_2 tension in the blood is the determining factor on which depends the intensification or weakening of erythrocytic adsorption of colloidal quinine. There exists, however, a certain ionic personalism, for an intramuscular injection in man or in sheep of ammonium chloride produces a stronger acidosis, while the intensification of adsorption is weaker than that of calcium chloride. This ionic individualism and other peculiarities are still under investigation.

THE erythrocytic adsorption of colloids is not a general phenomenon, that is to say I observed it only with one other colloid. See table 5.

The above table shows that neither the pH of the colloid nor its electric charge has any influence upon erythrocytic adsorption. It must be added that the gold, copper and silver hydrosols were prepared with the same technique and with the same stabilizing inter-micellary liquid; nevertheless, it was only silver that developed erythrocytic adsorption.

The erythrocytic adsorption of colloid-

Fig. 1

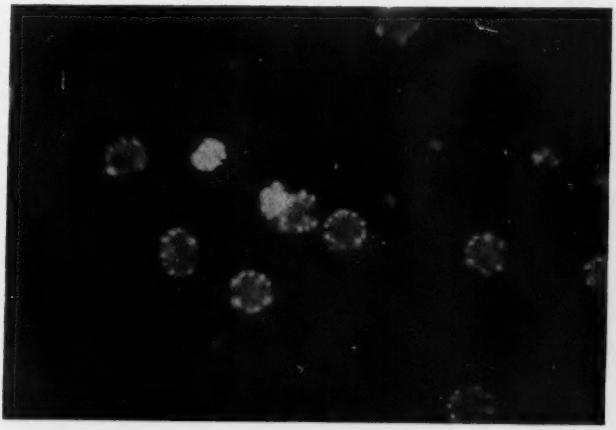


Table 5

Erythrocytic Adsorption
Influence of the nature of colloids and other factors

Colloids	*ph*	*Electric Charge*	*Erythrocytic Adsorption*
Gold hydrosol (electric)	6.78	(—)	(—)
Copper hydrosol (electric)	7.37	(—)	(—)
Silver hydrosol (electric)	6.90	(—)	+++
Copper morrhuate hydrosol (chemical)	7.80	(—)	(—)
Quinine hydrosol (electric)	7.70 (a)	(—) (a)	+++

al silver has the same characteristics as that of colloidal quinine, that is, it becomes intensified in acidosis and it disappears in alkalosis.

NOW I come to the pharmacodynamic application of these physico-chemical facts which give way to a better understanding of some heretofore obscure points in colloidology.

For example, now it can be understood why a blockade of the reticulo-endothelial system can not be obtained in certain cases, even though it is desired. The reason is that colloids that under normal conditions should rapidly pass through the blood and fix themselves in the reticulo-endothelial system may, under changed conditions, be retained in the periphery of the red corpuscles.

The antitoxic effect, one of the characteristics of colloids, is due to the fact that the colloid, when injected into the blood, adsorbs the toxins that it finds there and immediately brings them to the reticulo-endothelial system where the toxins and micelles are metabolized (8). The condition is, however, that the colloid does not develop erythrocytic adsorption because, in that case, instead of being taken away from the blood, the toxins would remain in the circulation, attached to the red corpuscles.

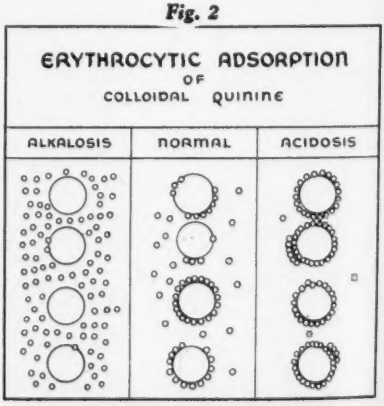
On the other hand, there are colloids whose bacteriostatic oligodynamic action is used, as in the case of colloidal silver. Actually, "water becomes markedly bactericidal after contact with metallic silver. Despite the fact that the concentration of silver ions reaches only one part in 20,000,000 heavy suspensions of bacteria succumb within a few hours." (9).

Under these conditions it is not astonishing that colloidal silver has given remarkable results in pneumonias and septicemias (10) (11); but so variable that they can not be generalized. This instability may now be explained and avoided by a humoral preparation that produces an acidosis assuring the fixation of the silver micelles by the red corpuscles, thus transforming the latter into carriers of the sterilizing agent, for an appreciable length of time and in all the parts reached by the blood.

IN malaria, the outlook is different, for the plasmodium localizes in the blood as well as in the reticulo-endothelial system. Colloidal quinine, when injected in acidosis, is adsorbed by the red corpuscles and does not reach the plasmodium localized in the said system, whereas the patient's alkalosis, a result of the paroxysm (12), makes the colloid immediately leave the blood, leaving the plasmodia that are found there free.

To make sure of these different destinies of colloidal quinine according to the patient's humoral conditions, I took advantage of the fluorescence of this alkaloid when it is exposed to Wood's light (13) and I photographed it. (a). The experiments were carried out with four dogs. Dog no. 1 was kept as control; dog no. 2 was given 20 cc. of colloidal quinine (0.02 Gm. of quinine) without any humoral preparation; dog no. 3 was in acidosis when he received the drug; and dog no. 4 was given the same dose in alkalosis.

Fig. 2



Acidosis was obtained by injecting intravenously 10 cc. of the following solution: citric acid 1.7; trisodium citrate 2.3; distilled water 100 cc. Previous experiments had shown that this solution raised the pH of the dog's blood to approximately 6.87 for a period of about 20 minutes.

Alkalosis was obtained in the dog by an intravenous injection of 50 cc. of an aqueous solution mol/2(53 °/₀₀) of $NaCO_3$, with pH raised to 9.0 by addition of $NaHCO_3$. The alkalosis of 7.7 appears and remains during the injection.

To test eventual diluting effects of the bicarbonated liquid that was administered, comparison was made between the quantity of red corpuscles per cubic mm. before and after the injection, without any appreciable difference being noted.

A piece of spleen, a piece of liver and a quantity of blood were taken from dog no. 1; 10 minutes after injection of the colloid the same items were also taken from the other dogs.

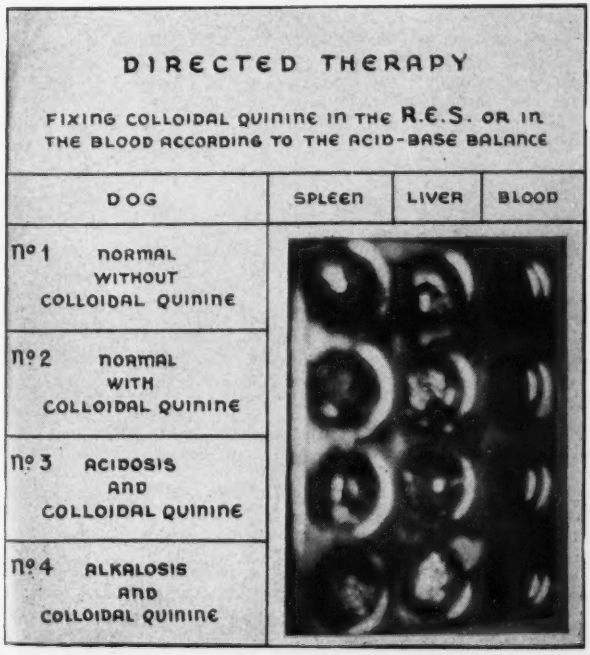
Fig. 3 is a copy of the photograph taken of all these samples when exposed to Wood's light in a dark room. For a correct interpretation of the fluorescence intensity it is necessary to discount the strong reflection of the light in various places, on the samples themselves as well as off them.

A remarkable difference is noted between the blood of the control dog and that of dog no. 2 which took the colloid without any humoral preparation. The blood of dog no. 3, which was in acidosis, appears slightly more intensive as to its quinine content, and the blood in alkalosis (dog no. 4) is identical with that of dog no. 1 that had not been given quinine.

The spleen of dog no. 3 shows much less quinine than that of no. 2, whereas no. 4 shows much more quinine. Such differences, even with greater distinctness, are observed in the livers.

I CONCLUDE from the preceding experiment (fig. 3) that absence of humoral preparation caused the colloidal quinine to be distributed between the blood and the reticulo-endothelial system (examples: liver and spleen), whereas in acidosis the colloid was concentrated in the blood; in alkalosis, finally, the colloid was concentrated in the Aschoff system.

Fig. 3


DIRECTED THERAPY
FIXING COLLOIDAL QUININE IN THE R.E.S. OR IN THE BLOOD ACCORDING TO THE ACID-BASE BALANCE
DOG
SPLEEN
LIVER
BLOOD
nº 1 NORMAL WITHOUT COLLOIDAL QUININE
nº 2 NORMAL WITH COLLOIDAL QUININE
nº 3 ACIDOSIS AND COLLOIDAL QUININE
nº 4 ALKALOSIS AND COLLOIDAL QUININE

When quinine acts on the parasite in the blood, it remains unknown whether it acts upon the "exo-erythrocytic stage" (14) since, actually, "although quinine has been employed for three centuries in the treatment of malaria, the basis for its use is as empirical today as it was when the Countess of Chinchon was given a decoction of chinchona bark" (9). The fact is that in the blood, besides the intraglobular life of the pasmodium, "there probably is an intermediate stage in the development of the parasite which is not passed in the erythrocytes" (14).

Is is, therefore, a fortunate event that by such a simple means as acidosis the colloidal quinine has its micelles fixed in the red corpuscles, precisely on their

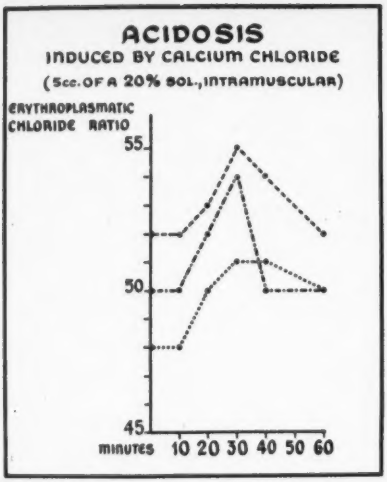


Fig. 4

periphery, for "much evidence has been accumulated to show that a drug may act on the surface of a cell" (15), so that the adsorbed micelle will bring the quinine to the surroundings in which the plasmodium is circulating, whether it be inside or outside the red corpuscles.

With the purpose of fixing the colloid in the circulation, that is, producing acidosis, among other means I tried in "anima vili" 5 cc. of 20% solution of $CaCl_2$, intramuscularly ([a]). The same experiment was repeated in "anima nobili" and its results are condensed ([b]) in fig. 4.

Fifteen minutes after administration of calcium chloride the colloidal quinine encounters the blood in an appreciable acidosis.

REFERRING to the parasites localized in the reticulo-endothelial system, we have to emphasize the capacity of quinine micelles to stimulate the said system of the liver, as exemplified with the Kupffer cells: fig. 5 shows two slices taken from the livers of two rats injected with trypan blue; only rat B, however, was given colloidal quinine injections. A comparison of both slices reveals hyperplasia of Kupffer's cells (16), as a result of the colloid.

† For the elaboration of this work there were carried out 280 electrometrical pH determinations, 274 determinations of alkali reserve and 263 determinations of the erythroplasmatic chloride ratio.

In spite of this encouraging result we should not neglect the old practice which has demonstrated that, although the spleen is easy to reach by specific medication, the liver needs additional treatment to stimulate its circulation. For such additional treatment calomel, sodium sulfate and other preparations have been used, according to successive vogues (17).

The hepatic adjuvant recently tried in malaria treatment is sodium dehydrocholate because of its high faculty of raising blood pressure in the hepatic artery, thus indicating an abundant supply of the blood which would better assure the arrival at the hepatic capillaries of the quinine injected at that very moment (18).

Now, it occurs that the hypertension of the hepatic artery as produced by sodium dehydrocholate is indeed intense but lasts from 3 to 5 minutes only, after which it enters immediately into a negative phase. On the other hand, this drug raises the blood pressure in the hepatic artery but lowers that of the portal vein.

AMONG the numerous drugs that have been used (19), sodium lactate is the only one which simultaneously raises pressures in both these blood channels of the liver, producing there a real hyperemia. Even though this drug has a less intense effect than dehydrocholate, it must be emphasized that its hyperemic effect lasts as long as 30 minutes during which time the bilirubin production is increased. Moreover, the lactic ion has also an actual tonic influence upon the hepaton (19).

In the particular case of preparing the effect of colloidal quinine upon the liver, sodium lactate has the advantage of not requiring the use of any additional alkalosis inducer, for it has by itself this property (20) as confirmed in the tests carried out in "anima nobili" by injecting in various patients, intravenously, 20 cc. of the molar solution of this salt ([b]). These results are seen in fig. 6, expressed by the erythroplasmatic chloride ratio (value of globular chloride divided by the value of plasmatic chloride (21) †.

It has thus been proved that the optimum in alkalosis is reached 20 minutes after injection.

IN order to test the hepato-hyperemic and cholecynetic power of sodium lactate and excluding the hypothesis that it might be due to the variation in the acid-

base balance, I carried out an experiment whose essence appears in fig. 7.

Microphotographs of the spleens and livers of four rabbits are put together, vertically, and confronted with photographs of the whole livers of the same rabbits, with special attention to the gallbladders. Rabbit no. 1 was left as control, no. 2 received calcium chloride, no. 3 sodium bicarbonate and no. 4 sodium lactate. All the injections were given intraperitoneally. Eight minutes after the injections were given, the animals were sacrificed. The spleen and liver vessels were ligated before these organs were extracted (†).

The remarkable cholecynetic power of sodium lactate becomes evident when we compare the four gallbladders: that of rabbit no. 4 shows itself so reduced in size that it seems like a buckshot. The lactate produced an intense blood afflux toward the liver† that will, of course, carry greater quantities of quinine and force the dilatation of the hepatic capillaries. This fact is important, for in the liver of malaria patients, "the capillaries are stuffed with parasites" (22).

Fig. 7 shows also that sodium bicarbonate does not provoke concentration of the blood in the liver, but, on the contrary, in the spleen.

This experiment, repeatedly performed with similar results, allows us to consider these facts as assured.

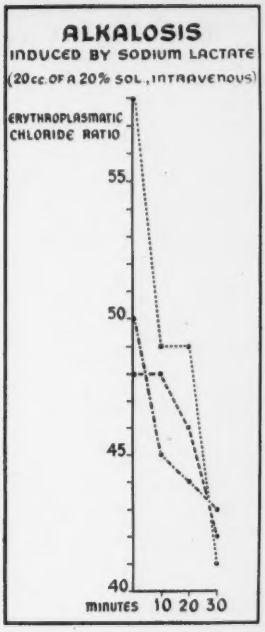


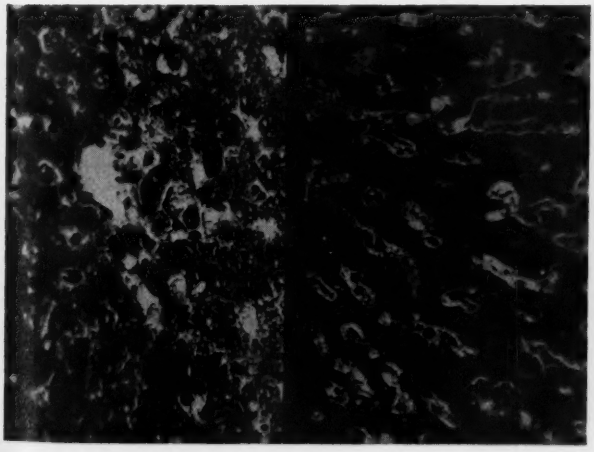
Fig. 6

THE extraordinary experimental field offered by a world at war gave the United States Navy the opportunity of observing that malaria, even when correctly treated, has always the tendency to provoke recurrences so that it may seem preferable to induce immediately controlled recurrences. For this purpose, fever attacks are artificially induced in natural hot vapor caverns, aiming at the dilation of the spleen and liver capillaries, thus sending toward the circulation the hematozoa that have escaped the effects of medication (23).

Personally, I think that this complicated physiotherapy which takes many days should better be substituted by a previous pharmacotherapy, namely, by the ingestion of bicarbonate which together with dilatation of the spleen capillaries produces also alkalosis, thus sending a concentrated charge of the sterilizing drug toward the spleen. Then follows an injection of sodium lactate which has

†The histologic slices were stained with hematoxilin, washed with ammoniacol and formol, stained again with acid fuchsin at 1%, washed in alcohol and differentiated with alcohol at 50°. Under these conditions, the erythrocytes appeared red and all the rest turned blue. With Zeiss violet-filter, photographs could be taken exclusively from the red parts.

Fig. 5



a similar effect on the hepatic capillaries. Finally, treatment has to be given to the blood whose parasites are meeting those that have been sent away from the organs, particularly from the spleen and liver.

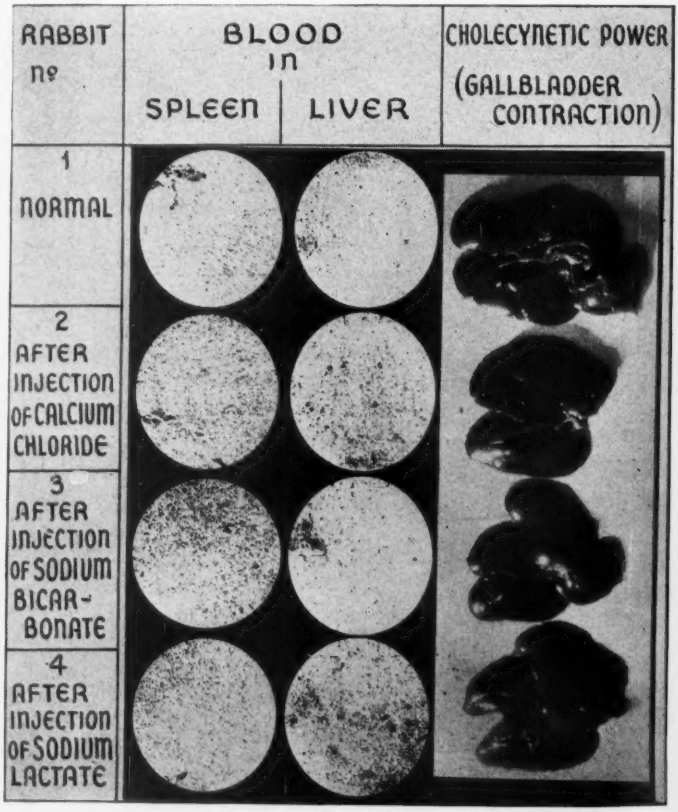
There are, however, other circumstances that have to be borne in mind in humoral preparation. For instance, if an acidosis is desired immediately after a malaria paroxysm, the normal dose of the drug should be sensibly increased, for in that moment the patient's organism is in alkalosis. It is, therefore, convenient to take advantage of natural opportunities which on the other hand succeed each other physiologically. It is known that a good alkalosis appears after a meal, especially when it was free of meat or other acidifying elements. The height of this alkalosis is reached within two hours after the meal. On the contrary, sleep and fasting are favorable conditions for acidosis.

Checking these factors, the cycle in which colloidal quinine may give the maximal benefit in malaria treatment will take the average time of 15 hours; see the cycle reproduced in fig. 8 ([b]).

This period, or at least its acidosic phase, must be chosen at a reasonable time in relation to paroxysms because the latter induce alkalosis, as mentioned before; "it is immaterial, however, in what part of the cycle quinine is given because the parasite in all stages is apparently susceptible" (9).

THE clinical aspect of the subject, concerning silver as well as quinine, is not part of this paper, for it views exclusively the pharmacodynamic standpoint and its main purpose is to make evident the possibility of what I call "directed therapy." This is something quite different from "chemotherapy" or simple alkalification or acidification through drugs, as for example that obtained with the use of mandelic acid. The name "chemotherapy" meant, originally, the supply of a drug intended to be fixed in the parasite only, without considering the cells of the host. "Directed Therapy," however, defines the possibility which the physician has to direct a drug so that it becomes fixed in determined tissues, cells or organs,

Fig. 7



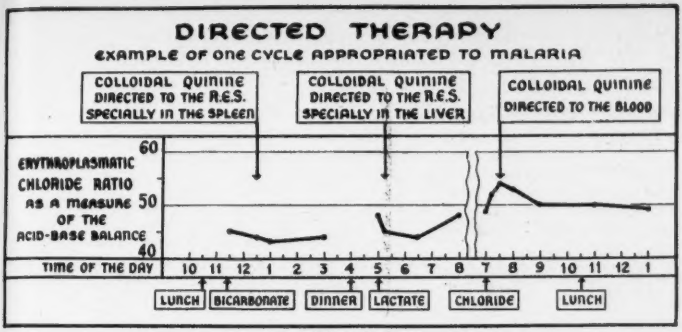

DIRECTED THERAPY
EXAMPLE OF ONE CYCLE APPROPRIATED TO MALARIA
COLLOIDAL QUININE DIRECTED TO THE R.E.S. SPECIALLY IN THE SPLEEN
COLLOIDAL QUININE DIRECTED TO THE R.E.S. SPECIALLY IN THE LIVER
COLLOIDAL QUININE DIRECTED TO THE BLOOD
ERYTHROPLASMATIC CHLORIDE RATIO AS A MEASURE OF THE ACID-BASE BALANCE
60
50
40
TIME OF THE DAY
10 11 12 1 2 3 4 5 6 7 8 7 8 9 10 11 12 1
LUNCH
BICARBONATE
DINNER
LACTATE
CHLORIDE
LUNCH

Fig. 8

or in other determined tissues, cells or organs of the same organism, owing to an adequate humoral preparation.

Conclusions

1—Under determined humoral conditions, erythrocytic adsorption of several lyophobic colloids is verified, impeding them in reaching their normal destination, the reticulo-endothelial system.

2—This fact, exemplified with silver and quinine, gives way to the so-called "Directed Therapy," consisting in the capacity of obtaining the voluntary fixing of a drug in determined tissues, cells or organs, or in other determined tissues, cells or organs of the same organism, owing to adequate humoral preparation.

3—"Directed Therapy" opens new prospects in infectious cases, as exemplified in the case of malaria.

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(b)—Dr. Guilherme Pires Filho, Hospital D. Pedro II, and his laboratory assistant Mr. Djalma Silva.

(c)—Dr. Helion Povoa, former Professor of General Pathology, University of Brazil, whose early death I report here with deep regret. His investigations in course have been performed by his assistant Dr. Antonio Teixeira de Mattos.

(d)—Dr. Joao Francisco de Souza, the coworker whose solidarity has been of greatest value to me.

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CANCER IN RELATION TO LIFE INSURANCE

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MY intention in presenting this paper is to call the attention of medical life insurance examiners to the fact that, in spite of our wide knowledge of all kinds of laboratory technics, we do not yet have a relatively simple and specific method for recognizing cancer in its earliest stages, as we can discover the presence of diabetes by testing the urine for sugar, or the beginnings of kidney disease by finding albuminuria, so that we must be constantly on the watch for any signs that will arouse our *suspicions* of malignant disease and thus cause us to make careful examinations, to confirm or disprove our suspicions.

Two recent reports, from authoritative sources,[1, 2] impress us with the increasing importance of cancer in the mortality figures.

For more than a decade, diseases of the heart, blood vessels, and kidneys have been the "Captains of the men of death," and they so remain; but in 1930 cancer was fourth on the list of killers, with a rate of 77 per 100,000, while in 1940 it had jumped over both pneumonia and tuberculosis into *second* place, with a rate of 103 per 100,000—an increase of 33.7 per cent.

This means that, today, out of every eight persons who die, one does so as a result of some form of malignant disease, and that more than 150,000 people die of cancer in the United States every year. Furthermore, it is estimated that more (nobody knows how many more) than 400,000 people—3 out of every 1000 of our inhabitants, young and old—now living in this country have cancer of some type.[3]

BEFORE preparing this paper I wrote to a few prominent insurance companies and fraternal organizations, asking them for the figures of cancer deaths in their groups, and to my surprise I received only a few replies.

The reply from Maccabees, of Detroit, Mich., gave me the following information:

	No.	Amount	Death Claims paid per 1000 Members	Claims paid per $1000 Protection
1940				
Cancer (all forms)	396	$375,331.25	2.33	2.13
1941				
Cancer (all forms)	444	$451,122.43	2.51	2.44

The reply from the Prudential Insurance Co. of America with information as follows:

Number of Deaths in the Ordinary Branch

Males

	1937	*1938*	*1939*	*1940*	*1941*
Cancer Deaths	2332	2321	2405	2562	2685
Total Deaths	18630	17863	18674	19334	19319
Percentage Cancer	12.5	13.0	12.9	13.3	13.9

Females

	1937	*1938*	*1939*	*1940*	*1941*
Cancer Deaths	945	955	953	1054	1065
Total Deaths	4970	4579	4906	5064	4886
Percentage Cancer	19.0	20.9	19.4	20.8	21.8

Information from the Polish National Alliance reported cancer deaths 1935 to 1939—1,395 for total amount of $817,000.

	1940	*1941*
Cancer Deaths	399	378
Total Deaths	2,804	2,869
Amount paid for cancer	$218,750	$248,501
Percentage Cancer	13	13.2

The reply from the Equitable Life Assurance Society gave me the following information:

E.L.A.S. Ordinary Death Rate per 100,000 Policies in Force.

Year	*All Causes*	*Cancer*
1941	881.5	124.6
1940	898.2	127.0
1939	860.5	111.4
1938	847.1	107.8
1937	870.0	107.6
1936	914.0	108.0
1935	872.2	103.0
1930	790.2	75.9
1925	776.3	77.3
1920	1034.9	96.8

We also have available the amounts of ordinary death claims paid over the past five years similarly classified.

E.L.A.S. Ordinary Death Claims Paid		
Year	All Causes	Cancer
1941	$54,370,000	$7,086,000
1940	54,787,000	7,971,000
1939	51,613,000	6,478,000
1938	53,733,000	6,730,000
1937	51,136,000	6,585,000

I wish to express my thanks to those groups which were so kind as to send me their experiences of the mortality rate of cancer for the mutual benefit of all.

IT is quite possible that some part of this increase is due to our improved methods of diagnosis, but it is doubtful if this is a very important factor. The increase in the number of older people is probably more significant, since it is well known that cancer is, predominantly, a disease of persons in or beyond middle age; so we may formulate the suggestion:

Most of the applicants for life insurance, who apply for large policies at, or beyond, the age of 40 years, should be suspected of having cancer until that condition is ruled out by the history or physical examination, whether or not they complain of any suggestive symptoms.

A general physical examination should be able to detect 43.4 per cent of early or suspicious malignant changes,[4] including those in the skin and accessible mucous membranes (mouth, pharynx, larynx, rectum, and vagina), breast, uterus, prostate, and testes. Fluoroscopic examination of the chest might help us to detect fairly early cancers of the lungs, pleura, and mediastinum, which might add about 5 per cent more. Roentgenographic studies, following a barium meal, might clear up about 20 per cent more of these cases. But this still leaves more than 30 per cent of the cases undetected, in their early stages, and in more than two-thirds of these the lesion is in the gastro-intestinal canal. It is to these that I shall devote particular attention.

Dr. Louis I. Dublin, of the Metropolitan Life Insurance Co., in reporting on the "Incidence of Gastric Cancer," in the *American Journal of Surgery*, 1934, said: "Cancer of the stomach is clearly the most important item in cancer mortality among males, being responsible for about one-third of all the annual male cancer deaths.

"For 1932 the recorded total deaths from cancer of the stomach in the United States was 16,000 for males and about 11,000 for females. Thus approximately 27,000 annual deaths in the population of the United States are from gastric cancer. On the basis of these figures, the crude death rate from gastric cancer in the general population of the United States is now about 21.6 per 100,000 of population."

The figures already quoted are, therefore, minimal and it may be necessary to increase them by one-half in order to get a true picture of the mortality situation. In keeping with this finding, it is Dr. Dublin's judgment that instead of 27,000, the annual number of deaths from cancer of the stomach and duodenum in the country at large is now more likely to be close to 40,000, or about as many as from bronchopneumonia, or coronary disease, including angina pectoris.

BEFORE going on with this subject, however, I want to call attention to a simple test for malignant disease of the cervix uteri, which can be performed in a few minutes, in his office, by any examiner, and should be applied to all women applicants beyond the age of 40, especially if they have borne children. It is known as the *Schiller test*,[5] and is carried out as follows:

After exposing the cervix and cleansing it, a generous quantity of Gram's iodine solution is applied and kept in contact with it for at least five minutes. Normal tissue turns a deep-brown color, while malignant tissue will appear much lighter, or even white, due to glycogen deficiency in the cancer cells.

It may also be worth while to mention that, in carcinoma of the *prostate*, the first symptom complained of may be *pain in the back and pelvis*, due to metastases to the bones, so if such pains are admitted, by a man in the "prostate age" group, roentgenograms should be made to determine the possible presence of malignant metastases.

In all examinations, the personal and family *history* is more important, particularly as regards cancer of the digestive canal and other internal organs, than many examiners realize.

SLYE demonstrated, a number of years ago, that a *tendency* to cancer, in mice, is definitely heritable and is more or less specific for certain organs and tissues (breast, stomach, etc.). Clinicians, also,

have recorded many instances where cancers have appeared in certain families for several generations.[6]

If the family history of an applicant reveals any deaths from causes that appear somewhat suspicious or ambiguous, the *details* should be looked into thoroughly, especially if the policy applied for is a large one.

Since cancer is most apt to occur in structures that have been subjected to long-continued *irritation* (most common sites are the mouth, stomach, breast, and anus), the presence or personal history of carious or broken teeth, chronic inflammations (as of the anus, cervix, stomach, etc.), repeated exposure to radium, x-rays, or irritating substances like tar and benzols, should arouse the examiner's suspicions and lead to an exhaustive investigation. So we may formulate another direct suggestion:

In all life insurance examinations, especially in cases where cancer is suspected, the personal and family history of the applicant should be looked into very carefully.

CARCINOMA of the *esophagus* is fifth in incidence of all malignant tumors. Eleven (11) per cent of all carcinomas in men, and 1.3 per cent in women, arise in the esophagus.

These neoplasms develop insidiously and are rarely diagnosed early, but are apt to metastasize early and offer poor prospects of cure.

The sudden onset of *dysphagia*, in a previously healthy person between 40 and 70 years old, is presumptive evidence in favor of carcinoma of the esophagus.[7]

Carcinoma of the *stomach* accounts for one-third of all malignant tumors (two-thirds of all cancers in men, and one-half of those in women, are in the digestive tube). It is more common in men than in women (65:35), and is commonest between the ages of 40 and 70 years. This is not astonishing when one remembers the large preponderance of peptic ulcers in men, as compared to women, and the generally accepted belief or conviction that such ulcers are always potential sites for the development of cancer.

The symptoms of carcinoma of the stomach are not definite nor typical, and may vary greatly, depending upon the site of the lesion, the age and sex of the patient, and other considerations. The fact that 42 per cent of all cancer patients are habitually constipated may be significant.

When a man past the age of 40 begins to complain of fullness and discomfort after meals; slight anorexia, especially for meats; and loss of strength and weight; and when he responds slightly or not at all to medical treatment, the doctor should suspect a malignant tumor and study the patient intensively, on that basis, until that suspicion is confirmed or disproved. Perhaps, when large policies are involved, such studies should include roentgenography, gastroscopy, and possibly peritoneoscopy.

In any case, the *stools* should be examined, several times, for *occult blood* (the applicant being kept, meanwhile, on a meat-free diet), and the *stomach contents* should be examined for blood, free acid, Boas-Oppler bacilli, and possible malignant cells. Large hemorrhages are rare in gastric carcinoma, unless secondary ulceration occurs.

Vomiting, in gastric carcinoma, occurs only if the pylorus or the cardia is obstructed; and an examination of the vomitus should readily show from which level it has come.

Pain is often absent in the early stages of cancer of the stomach, unless there are adhesions or metastases to other organs, and these usually develop fairly late.

If a *mass* is palpable in the epigastrium, especially if it moves with respiration (which generally indicates that it is in or attached to the liver), the case is not an *early* one of any type, and a policy should be refused to any applicant showing this sign, unless and until the benign character and curability of the tumor have been conclusively demonstrated.

The prognosis of gastric carcinoma is not good, although, if the process is *incipient*, many persons so afflicted may well live the length of time that is required to make a policy incontestable. (The only types of cancers that have an *average* life expectancy of two years or more after diagnosis are those of the skin and breast). In the United States, in 1932, the deaths from this cause numbered 40,000, and that figure is, no doubt, higher now. A few "cures" lasting more than 5 years have been reported, but they are decidedly rare.

What may possibly (but by no means certainly) prove to be a valuable aid in diagnosing cancer of the stomach, by

means less severe than gastroscopy and less tedious than a series of gastro-intestinal roentgrams following a barium meal, was revealed when the Advisory Cancer Council, a few months ago, approved a grant of funds to carry on studies inaugurated by Dr. Edmund N. Goodman (who is now in the Army) and continued by Dr. Allen O. Whipple of Columbia University.

This test (in sketchy outline, since no details are now readily available) is made by measuring differences in the electrical potential across the stomach membranes when milk is in that viscus. It may prove to be impracticable for use in life insurance examinations, but is worth watching.

SINCE it is wholly impossible to determine, in advance, which of the younger applicants will later develop cancer, and the most careful medical examiners cannot always detect existing cancers in their earliest stages, the *curability* of various types of malignant tumors is of interest in estimating probabilities of death and in determining the amounts of extra premiums to be charged, if it is deemed advisable to issue a policy after a so-called "5-year cure."

Some companies will accept carefully selected cases after five years of apparent recovery on payment of an extra $30.00 per $1000 per year until ten years have elapsed following operation without recurrence.

The more easily a malignant tumor can be seen, and the more accessible it is to surgical intervention, the better are the chances for a 5-year cure. Figures presented by Hoffman,[8] in 1934, showed that the rate for skin cancers was 60 per cent; those of the lip, 50 per cent; of the uterus, 10 per cent; breast, 9 per cent; larynx and testis, 5 per cent; rectum and intestine, and bone sarcoma, 2 per cent; stomach, liver, gallbladder, prostate, and kidney, 1 per cent. These figures have, no doubt, been improved somewhat during the past eight years, but probably not to any very notable degree.

Precancerous conditions are many, and examiners should always be on the lookout for them. Leukoplakia is one of the most common precursors of malignant disease, and tertiary syphilitic lesions are apt to become malignant. All gastric ulcers should be considered as potential stomach cancers. Papillomas and blue-black moles are frequently the sites of highly malignant tumors. Senile keratoses and those of occupational origin are frequently the beginnings of skin cancers.

In suspicious cases, where the applicant is willing to submit to a biopsy, it should be made, if the examiner feels sure that this will not involve danger of disseminating cancer cells. Such accidents can be obviated or minimized by using an electric cautery knife, loop, or punch for removing the specimen.

Although there is, at present, no sign or test that will permit us to recognize, unfailingly, an incipient cancer of the stomach or upper bowel, there is one occurrence that takes place fairly early in most such cases, and that is *bleeding*.

If there is a hemorrhage, even of small extent, in these localities, the blood is partially digested and passes down into the colon and rectum as a black, tarry mass, and this permits the formulation of a third general suggestion:

Any applicant who is not taking any preparation of iron or bismuth, and who admits the passing of tarry or black stools, should be considered as having a cancer of the stomach or upper bowel until the contrary has been clearly proved.

In this paper I have formulated three suggestions that may help every medical examiner to detect the early stages of carcinoma.

In conclusion I honestly believe that, if all medical men, whether medical examiners or not, were informed that after two years since an insurance policy was issued, the policy is incontestable and the company or fraternal organization must pay the full amount, those doctors who put the blame for death on the heart would give more correct causes of death and, by doing so, I believe that cancer would occupy the first place as the cause of death, because every "heart failure" is necessarily a cause of death, but not every heart failure is due to heart disease.

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—Concluded on page 312

MISCELLANY

CHINESE MEDICINE

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CHINESE medicine developed in the same way as Chinese literature and art: the ideas are presented mainly by insignificant details, so that the essential facts remain obscure. However, the original concept of Chinese medicine is of great historical interest.

Chinese medicine is characterized by stationary status, formalism and pedantry. As early as 2697 B. S. Huang-ti composed medical works which are considered to be the Chinese classics. These works were done in lacquer on palm leaves. Chinese anatomy and physiology were dominated by Huang-ti's system. In 1122 B. C. Chin Yeuh Jen compiled a work on the arterial and visceral systems. In A. D. 1644 the Emperor Chien Lung published an *Encyclopedia of Chinese Medicine*. About the same time Sheng Tung wrote a treatise on osteology.

THE early Chinese anatomists described mainly splanchnology, angiology and physical anthropometry in accordance with their embryonic knowledge. The ancient Chinese medical authors believed that there are two cosmic principles: light, heat and life on one side, and darkness, cold and death on the other side. These principles are distributed to various parts of the organism. The functions of the organs are mainly as follows: the viscera eliminate, the liver stores the blood which contains the soul, the heart stores the spirit, the spleen is the source of thought, the lungs of energy, the kidneys of the will. Huang-ti in 2697 B. C. described measurement of the bones and digestive tracts. Teng Chiano in A. D. 1644 advanced the knowledge of regional anatomy.

The ancient Chinese surgeons performed castration, dry cupping and massage but not venesection. In the diagnosis of diseases they examined the pulse of the radial artery in the mode of striking the keys of a piano. They used numerous drugs including rhubarb, aconite, opium, sulfur, mercury and arsenic. They also made use of many preparations taken from the animal world. The ancient Chinese had knowledge of preventive inoculation against smallpox (Garrison). Modern Medicine, however, revolutionized medicine in China mainly as a result of the establishment of numerous medical schools and hospitals by foreign and Chinese governments.

THE late Dr. William H. Welch, leading American physician, in a letter to Colonel Fielding H. Garrison, dated November 13, 1921, presented an account which he had copied on his trip to China, from the journal of a British Dr. Gray, of the latter's experience with a native Chinese physician. It reads as follows:

"A few days ago (i.e., May 1910) while walking in the Tartar City (Peking) I stopped at a Chinese doctor's stall and asked him if he would prescribe for me as I was feeling out of sorts. He said if there was anything wrong he would soon find out, and at once began feeling my radial pulse, first the left and then the right, taking about five minutes in turns with his first, second and third fingers, then all together, without asking any questions. He then wrote a prescription of which the following is a translation:

Prescription

Powdered Bramble seed
Powdered Peony
Powdered Plaintain Branch
Powdered Water Chestnut
Powdered Bamboo Shoots
Powdered Pine Bark
Powdered Olive Tree Bark
Powdered Ginger Root Bark

This peculiar form of examination and treatment was characteristic of the Chinese physicians in the beginning of this century. However, they have gradually made some progress and improved both their methods of examinations and treatment.

CONTEMPORARY PROGRESS

RHINOLARYNGOLOGY

Lymphoid Hyperplasia of the Nasopharynx

A. R. HOLLENDER and P. B. SZANTO (*Archives of Otolaryngology*, 41:291, April 1945) report a study of the lymphoid tissue in 131 autopsy specimens from adults twenty to seventy-five years of age and over. Every specimen included Waldeyer's ring or its remnants. Hyperplasia of the nasopharyngeal tonsil was found in 9 specimens; in 4 in subjects over 70 years of age. In one of these specimens, in a woman 75 years of age, there was involution of the palatine tonsils and moderate development of the lingual tonsils. Histological examination of the hyperplastic nasopharyngeal tonsil showed a morphologic picture practically the same as that of adenoid vegetations in childhood. Partial involution of the nasopharyngeal tonsil was a common finding. Hyperplasia of the tubal tonsil was less common than hyperplasia of the nasopharyngeal tonsil (4 specimens). Hyperplasia of the nasopharyngeal tonsil does not necessarily cause symptoms in adults. This depends primarily upon the size of the nasopharyngeal vault; if this is large, so that hyperplasia of the lymphoid tissue does not cause pressure, no symptoms of obstruction will result. Hyperplasia of the tubal tonsil, unilateral or bilateral, is of importance because of its relationship to the ostia of the eustachian tube. Although such hyperplasia has been recognized as a cause of deafness in children, its possible significance in the impairment of hearing in older persons does not seem to have been appreciated. In cases where there was hyperplasia of the nasopharyngeal and tubal tonsils, no relation was found between such hyperplasia and the degree of development of the lymphatic tissue of the spleen and Peyer's patches in the intestine. Also no correlation was demonstrated between hyperplasia of the lymphoid tissue of the nasopharynx and general pathologic conditions. On the basis of these findings the authors conclude that there is "no general rule" regarding the involution of lymphoid tissue in Waldeyer's ring; they consider that it is "reasonable to assume" that certain constitutional factors are responsible for the variations in the development and involution of this lymphoid tissue.

COMMENT

To the otorhinologist who routinely uses the nasopharyngoscope in the examination of patients the presence of "adenoids" in a large number of adults is well known. It is not unusual in our experience to find this lymphoid tissue causing eustachian tube difficulty.

L.C.McH.

An Adaptation of the Displacement Principle for the Introduction of Gases into the Sinuses

A. W. PROETZ (*Annals of Otology, Rhinology and Laryngology*, 54:91, March 1945) describes a modification of his displacement method making it possible to introduce gases into the sinuses. This modification was introduced because effective vasoconstrictors in gaseous form are now available, but with even the best of modern inhalers, the drug does not penetrate the ostia, especially when they are blocked with secretions. The apparatus used consists of a bomb-shaped container with a cotton cylinder saturated with the drug to be used, similar to most inhalers. A small hole is drilled in each end of the container. The same pumps, the same olive tip and the same pressure are used as for displacement with fluids. The hole at the distal end of the container must not be larger than 1/64 inch in diameter, and it may be smaller, i.e., a pin hole. The hole in the proximal olive tip end, which is inserted in the nostril, should be larger than this. Intermittent

suction is applied at one nostril, while the patient keeps the mouth open and the velum palati in the "k" position, as in the displacement method with fluids. Instead of closing the opposite nostril with the finger, however, the perforated olive tip of the container is inserted snugly into this nostril. The negative pressure draws the fumes into the nose, while at the same time it evacuates part of the air from the sinuses. When the negative pressure is released, small quantities of the "vapor-laden" air are carried into the sinuses. The pressure is applied several times as in the original displacement method. This procedure is carried out with the patient in the erect position, not in the usual displacement position, as gravity plays no role. As the volatile constrictor drug employed with this method may be retained for a time in the sinuses, it should be selected with care. The author has employed a preparation of 2-aminoheptane, which has been found to have "a minimal systemic effect."

COMMENT

From our experience with these volatile constrictors we would be fearful of giving a patient a large overdose by administration with this method. Certainly a very profound shrinkage of the nasal mucous membrane would be expected from such therapy.

L.C.McH.

Irrigation of the Maxillary Sinus by Way of the Middle Meatus

O. E. VAN ALYEA (*Annals of Otology, Rhinology & Laryngology*, 54: 298, June 1945) advocates the use of the middle meatus for irrigation of the maxillary sinus in all cases. His anatomic studies have shown that in approximately 55 per cent of cases the maxillary ostium or an accessory ostium is readily available for catheterization by this route. The author's technique of irrigation of the maxillary sinus is as follows: The middle meatus only is anesthetized; the membranous area is carefully probed for an accessory opening. The tip of the cannula is then brought forward into the hiatus semilunaris between the bulla and the unicate process; as the space between these two structures narrows, the tip of the cannula is rotated downward and should pass into the normal ostium. Entrance into the ostium is prevented if the hiatus is too narrow at the point adjacent to the ostium, or if rotation of the cannula is prevented by a large turbinate. If the ostium is not entered easily with little probing, a cannula with a sharp point is substituted for the dull-tipped cannula, and the membranous wall penetrated. The usual point of penetration is just above the superior border of the inferior turbinate near its posterior third; the opening is little more than 2 mm. in diameter and heals quickly. Irrigation of the maxillary sinus is not indicated in the early stages of an acute attack of sinusitis, but is of value in the later stages when tissue edema has subsided. In chronic maxillary sinusitis, irrigation of the sinus is of value as an adjunct to other methods of therapy, and especially as a diagnostic aid and for checking the results of treatment. For this latter purpose iodized oil is introduced into the sinus for roentgenological study. With the method described repeated irrigations can be easily done.

COMMENT

We agree in all particulars with Doctor Van Alyea and might add that we have rarely

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found it necessary to use a sharp pointed cannula as the dull tipped cannula usually penetrates the membranous wall rather easily.
L.C.McH.

Anesthesia for Tonsillectomy Induced by Intravenous Administration of Pentothal Sodium

S. L. FOX and S. ROCHBERG (*Archives of Otolaryngology*, 41:439, June 1945) report the use of intravenous anesthesia with pentothal sodium for tonsillectomy in adults. This type of anesthesia had previously been used for reducing fractured noses, for mastoidectomy, and for plastic operations around the nose and ear. The major cause of failure of intravenous anesthesia for operations on the throat has been the difficulty of maintaing an adequate airway throughout the operation. This has been overcome by the use of the Davis mouth gag with detachable tongue blades of various sizes. With this gag properly applied, the tongue is held downward and forward, the mouth is kept open, and oxygen or ether or nitrous oxide can be administered. The tongue blade employed should be of the correct size so that its tip fits into the hypoepiglottic sulcus and the tongue is depressed so as to insure an adequate oropharyngeal airway; the epiglottis is often visible if the tongue blade is inserted correctly. Intravenous pentothal sodium anesthesia has now been employed in approximately 200 adenotonsillectomies. The youngest patient in the series was 13 years of age, but of large build. All patients were given a hypodermic injection of ¼ to ⅓ grain of pantopon and 1/150 grain of atropine sulfate one-half to one hour before operation. The patient was placed in the head-low (Trendelenburg) position; this position tends to prevent laryngeal spasm by preventing secretions from the mouth and throat from coming in contact with the larynx. The throat suction apparatus was also connected before the anesthetic was given, so that secretions or blood could be promptly aspirated. As soon as sufficient pentothal had been administered to put the patient "profoundly asleep", the Davis mouth gag was inserted. The operation was not begun until the throat muscles were quiet and the pharyngeal reflex abolished. Sufficient pentothal was given to keep the patient asleep throughout the operation. The throat suction apparatus was employed by the assistant as necessary to keep all secretions away from the hypopharynx. All bleeding was completely controlled before the patient was removed from the operating table. A breathing tube was placed in the mouth at the end of the operation to maintain an adequate airway until the pharyngeal reflex returned. When the patient was returned to bed, he was kept in a semilateral position with a pillow under the chest, and the head extended. A 2.5 per cent solution of pentothal sodium has been used in preference to the 5 per cent solution as the authors have found that slightly less of the drug is required with the weaker solution. From 1.0 to 1.5 gm. of pentothal sodium has been the average dose required for tonsillectomy in adults. In the later cases in this series, nitrous oxide and oxygen, in approximately equal parts, have been given by way of the mouth gag throughout the operation. This reduces the total dose of pentothal. In every case in the series, the operation was successfully completed under pentothal sodium anesthesia, supplemented only by nitrous oxide. Postoperative complications were few; there was no postoperative vomiting; and postoperative sedation was very rarely required. Fluids were given "almost immediately" after operation, preventing dehydration and fever.

COMMENT

We have had several frightening experiences is using pentothal sodium anesthesia for procedures about the throat or larynx and are inclined to be extremely cautious in using an anesthetic agent where the margin between surgical anesthesia and respiratory depression is so extremely narrow. We agree with the authors that maintenance of an adequate oropharyngeal airway is essential in the use of any general anesthetic agent.
L.C.McH.

OTOLOGY

Penicillin in Mastoiditis and its Complications

F. J. PUTNEY (*Archives of Otolaryngology*, 41:247, April 1945) reports the use of penicillin in the treatment of mastoiditis and its complications. Adequate

surgical treatment was required in almost all cases to effect a cure, but the administration of penicillin caused rapid improvement of symptoms. At first penicillin was given intravenously, but the author has found intramuscular administration to be more satisfactory for most otologic infections, although in an occasional case of unusually severe infection, continuous intravenous drip may be necessary. The usual dosage for intramuscular administration was 25,000 units every three hours, reduced to 15,000 units every three hours, when the patient showed definite improvement. Penicillin was also used locally after operation, by irrigation through a rubber Dakin tube after primary closure of the wound, by irrigation to the open mastoid cavity, or by packing the open wound with gauze impregnated with penicillin, changing dressings daily. In 4 cases of uncomplicated mastoiditis local irrigations of penicillin were employed after simple mastoidectomy without intramuscular injections; the wound healed promptly in all cases. However, in complicated cases of mastoiditis, penicillin is given by intramuscular injection as well as employed locally. The solution employed for local application contained 250 units of penicillin per cc. Ten cases of mastoiditis are reported, 6 complicated by lateral sinus thrombosis, one of acute purulent mastoiditis in which cure was not effected by penicillin alone and mastoidectomy was necessary, one case complicated by petrositis, one by epidural abscess and one by cerebellar abscess. In all of but one of these cases cure was effected by a combination of the administration of penicillin systemically, adequate surgical procedures, and local application of penicillin in the wound. In one case in which the diagnosis of lateral thrombosis complicating mastoiditis was made, the patient was cured by intramuscular injections of penicillin alone; but as the diagnosis was not confirmed by operation, the author considers that the result in this case is not decisive.

COMMENT

We wish to commend the author for stressing in his report regarding the use of penicillin the necessity of adequate surgical treatment. There is no question but that penicillin reduces morbidity and at times saves lives which would otherwise be lost from the complications of mastoiditis.

L.C.McH.

The Use of Otosmosan in Otology

S. J. KOPETZKY (*Laryngoscope*, 55: 216, May 1945) reports the use of a combination of urea and sulfathiazole (otosmosan) in the treatment of suppurative otitis media. This preparation is a chemical combination rather than a mixture of its two principal components; it contains 10.82 per cent of urea and 9.68 per cent of sulfathiazole with 1 per cent benzocaine in absolute glycerine as a vehicle. Otosmosan was applied locally in the cases reported by being instilled into the affected ear with the patient lying on the opposite side so as to keep the affected ear up to hold the solution. The drug was retained in the ear for about fifteen minutes, and was then allowed to flow out, without drying. Treatment was repeated every twelve hours, the patients being instructed in making the applications correctly. This method was employed in 21 cases of chronic purulent otitis media, in which the discharge was of long standing. The ear became dry in 7 cases after treatment for one week to one month in most cases, only one requiring five months' treatment. In 6 cases the discharge was diminished but the ear did not become entirely dry. Four patients did not return for re-examination. The treatment was also used in 4 cases in which the discharge had persisted for several years after a simple mastoidectomy. The ear became entirely dry in 3 cases; the fourth patient showed much improvement after a month's treatment. In 11 cases of persisting discharge after acute suppurative otitis media, in which mastoidectomy had not been done, the ear became dry within a month in 6 cases (in 4 of these within a week); 5 patients did not return for re-examination. In 16 cases in which ear discharge had persisted after radical mastoidectomy, the ear became dry under treatment in 9 cases; 3 patients showed definite improvement; 4 did not return for re-examination. A number of patients complained of pain in the ear after the application of the sulfa and urea combination. This can be prevented by avoiding the use of water with the preparation. This treatment should not be used in patients showing an idiosyncrasy to sulfa drugs, nor if there are any symptoms of intracranial complications.

COMMENT

Whether this preparation is a great deal

better than other methods of therapy for draining ears remains to be proven by observation of many men over a long period of time.

L.C.McH.

The "Unsafe" Ear

J. F. BIRRELL (*Edinburgh Medical Journal*, 52:213, June 1945) states that the regulations of the British Army exclude from service men with postero-marginal, postero-superior or attic perforations of the ear drum, as these perforations indicate erosion of the mastoid bone or involvement of the attic. Persons with central perforations of the ear drum are accepted for home service. In the author's experience in a General Hospital in North Africa and Italy during the War, however, he has found that there was a larger percentage of soldiers with the "unsafe" type of chronic otitis media than with the "safe" type. This is probably due to the fact that in the "unsafe" type of chronic otitis media, the perforations are marginal and small, the secretion scanty, and the discharge often intermittent, so that diagnosis is more difficult, and the condition more apt to be overlooked in routine examinations. In 164 cases of chronic otitis media of the "unsafe" type studied, 96 had had otorrhea since childhood; the perforation was most frequently of the postero-marginal type. A deficiency in hearing had been noted by 142 of these patients, but the hearing loss was rarely great. The treatment of this type of chronic otitis with mastoid involvement must be surgical, preferably the modified radical mastoid operation; hearing is improved by this operation in the majority of cases, and the danger of complications obviated; whether a dry ear will be obtained depends upon adequate after-treatment.

COMMENT

Ears with postero-marginal perforations, especially with chronic discharge, even though quite scanty, are well known to be unsafe ears. We are interested in the author's observation that such ears are apt to be overlooked in routine examination. It is our feeling that mass production medicine necessitates a great many "routine examinations." It behooves doctors to take great care lest "routine" becomes synonymous with "incomplete" and "careless."

Treatment of Deafness, Ear-Noises and Dizziness by Hypothermic Therapy

S. QUISLING (*Journal-Lancet*, 63:219, June 1945) advocates the use of cold (hypothermic) therapy in the treatment of eighth nerve disturbances causing deafness, tinnitus and dizziness. Cold has a primary vasoconstrictor action, followed by vasodilatation; it also reduces the metabolic rate; this favors increased fluid transfer to and from the endolymph. Cold therapy has been used in otosclerosis, Ménière's disease, and in other forms of eighth nerve disturbances due to faulty blood supply and/or pressure of endolymph in the labyrinth. The use of cold in these conditions is based on the following observations: The phenomenon of paracusis Willisii can be induced by cold; the cochlear as well as the vestibular division of the eighth nerve is sensitive to cold; decreased blood supply to the labyrinth causes deafness, head-noises and dizziness. The method of treatment employed consists in freezing the skin of the area over the mastoid and petrous portion of the temporal bone with ethyl chloride spray, which is applied until the skin blanches. In about one-half to one minute, the skin is warmed by the hand of the operator. With very thin-skinned patients, the skin may be warmed as soon as it blanches. Treatment is repeated two or three times over each ear area. Treatments are given once or twice a week for six to twelve treatments. If definite improvement results, treatments are continued until the maximum degree of improvement is obtained. Treatments may then be repeated at monthly or at longer intervals to maintain the improvement. In the author's experience, this treatment has given good results in more than 70 per cent of cases of "eighth nerve irritation." Three illustrative cases of otosclerosis, 2 cases of Ménière's disease, and one case of eighth nerve deafness due to chronic purulent otitis media are reported, in all of which cold therapy gave satisfactory results.

COMMENT

We are unable to understand the benefit obtained by this type of therapy on a physiological or pathological basis; we are inclined to doubt that the application of cold to the skin over the mastoid will have any lasting local effect upon the labyrinth.

L.C.McH.

The Bárány and Galvanic Tests, Their Value in the Diagnosis of Labyrinthine and Intracranial Disease in the Presence of Suppurative Otitis Media

B. RACHLIS (*Archives of Otolaryngology*, 41:422, June 1945) reports 3 cases of otitis media in which the vestibular tests were of definite value in establishing the neurological diagnosis and indicating the site of the complicating lesion. A fourth case is noted in which there was a tumor of the cerebellopontile angle associated with a chronic otitis media. The vestibular tests in this case were suggestive of the true nature of the lesion, but were misinterpreted. It should be noted that not all intracranial disease in the presence of disease of the middle ear is necessarily of otitic origin. The Bárány tests are an adjunct to otologic, neurologic and neurosurgical diagnosis. They supply a method of examining the vestibular mechanism, including the labyrinth, the vestibular nerve and their central connections. When the results of the Bárány tests are definitely positive or definitely negative, they are of special value and significance in differentiating between an infratentorial and a supratentorial lesion, and also in establishing the diagnosis of a lesion of the cerebellopontile angle. The Bárány tests are not infallible, nor do they establish a definite diagnosis; the final diagnosis depends on a careful history, complete physical examination with a study of the eyegrounds, in addition to vestibular tests. In some cases more than one lesion is present, as for instance, an intracranial lesion with degenerative labyrinthitis, which still further confuses the diagnosis. The galvanic tests, though only qualitative, are of value in cases in which the Bárány tests cannot be used, or to differentiate between a labyrinthine and a retrolabyrinthine lesion, when the Bárány tests do not elicit vestibular responses.

COMMENT

It is sometimes very difficult to determine how much testing of the labyrinth is of practical value and how much is of only theoretic value in patients with otologic and neurologic lesions.

L.C.McH.

PEDIATRICS

Blood Pressures in Children Between the Ages of Five and Sixteen Years

A. W. GRAHAM, E. A. HINES, JR. and ROBERT P. GAGE (*American Journal of Diseases of Children*, 69:203, April 1945) report a study of blood pressure in 3,500 children, followed year by year from the age of five years to that of sixteen years. Twenty-five thousand determinations of blood pressure were made, all by one physician using a constant technique. These studies show linear increase of both systolic and diastolic blood pressure with each year of age. The average blood pressure readings of both sexes were within 1 unit of each other at each year of age. The modal systolic pressure was 52 mm. at the age of five years and 122 mm. at the age of sixteen years; the modal diastolic pressure increased from 52 mm. at the age of five years to 62 mm. at sixteen years. The variations in blood pressure increased with age, and greater variations were observed in girls 10 to 13 years of age than in boys in the same age period. The authors expect later to make a detailed study of the blood pressure readings in the same group of children in relation to the associated diseases of childhood.

Correlation of Symptomatology with Enterozoic Parasitism in Children

R. L. BROWN (*Journal of Pediatrics*, 26:291, March 1945) reports stool examinations on 512 children admitted to the Philadelphia General Hospital Pediatrics Department; repeated examinations were rarely made in this series. The stool examinations included both macroscopic and microscopic studies. Enterozoic parasites were found in 345 of the 512 children examined, or 67.3 per cent. *Entamoeba histolytica* was found in the stools of 41 children; 7 of these children had acute, moderately severe, nonfulminating dysentery; intermittent constipation and diarrhea and some degree of malnutri-

tion and generalized abdominal tenderness, especially over the right iliac fossa, were present in all these 7 cases. Eleven patients with *E. histolytica* gave a history of chronic recurrent diarrhea; 9 of these 11 children were underweight and 4 showed moderate abdominal tenderness in the right lower quadrant; only cysts of *E. histolytica* were found in the stools in these cases. Emetine, carbarsone or both, in dosage according to the age of the patient gave satisfactory clinical results in all cases with symptoms due to *Entamoeba histolytica*. Of 165 children with *Giardia lamblia* in the stools, 15 had acute generalized abdominal pain, intermittent diarrhea and constipation; excess mucus and detectable blood were found in the stools of 3 of these patients; all these 15 children had moderate flatulence and were irritable and inattentive. Twenty-three other children with *Giardia* in the stools gave a history of repeated diarrhea. Atabrine relieved the acute symptoms and decreased the number of *G. lamblia* in the stools. Two of 3 children with *Ascaris lumbricoides* in the stools had generalized abdominal pain and tenderness, with "episodes" of colicky epigastric pain and gave a history of similar episodes; caprokol (hexylresorcinol) relieved the symptoms. Twenty of 21 children with *Enterobias vernicularis* had pruritus ani, with disturbed sleep, irritability and inattentiveness. Symptoms were relieved by treatment with gentian violet and protection against reinfection while the patients were in the hospital. Of the 6 patients with teniasis, 4 had flatulence, intermittent constipation and diarrhea, abdominal tenderness and erratic appetite; all these 4 children and one other in this group showed malnutrition. Male fern was effective in the treatment of all these cases. In the entire group of children showing enterozoic parasites in the stools, specific symptoms due to the parasites were present in only 7.7 per cent. It was noted that recurring upper respiratory infections occurred more frequently in the parasitized than in the nonparasitized children.

The Prevention of Measles With Gamma Globulin

H. E. KLEINSCHMIDT *(Archives of Pediatrics,* 63:167, April 1945) reports that gamma globulin from human serum is now available in large quantities as "a by-product" of processing of serum albumin for the armed forces from blood collected under well-controlled conditions by the American Red Cross Blood Donor Service. Gamma globulin contains antibody globulins that are standardized so that the concentration of antibody is 25 times that of the "plasma pool" from which it came. Gamma globulin is employed for prevention of measles in a dosage of .08 to 1 cc. per pound body weight, given as soon after exposure as possible; and for modification of the disease in ¼ the preventive dose on or about the fifth day after exposure. In New York City the records show that the incidence of measles in children exposed in the household to a case of the disease is 83 per cent when no immunization has been attempted. In a series of 814 children (six months to six years of age) who were "household contacts," the injection of 2 cc. gamma globulin on the first to the tenth day after exposure prevented measles in 78.7 per cent; the remainder developed measles of mild to moderate type, none severe measles (as reported by Greenberg et al. in 1944). The results with gamma globulin were superior to those obtained with placental globulin in a control series. Gamma globulin is now being made available for civilian distribution by the Red Cross to state and local health departments and through these departments to physicians, hospitals and clinics.

Intratibial Infusions in Children

R. D. SEMSCH and A. V. STOESSER *(Journal-Lancet,* 65:194, May 1945) describe a method for intratibial infusions in children, which is a modification of the method described by Arbeiter and Greengard in 1944, employing the Schleicher sternal aspiration needle with metal adaptor. The tibia has been chosen for interosseous infusion because the leg can be easily stabilized making it very difficult for the patient to disturb the needle, and also because the marrow cavity of the tibia is large, permitting an inflow of fluid at almost any given rate. For intratibial infusion, a well-padded board with a heel support is employed, to which the leg is fixed with two-inch elastic bandage. The site used for the puncture is about 1½ to 2 cm. below the insertion of the tendon of the quadriceps muscle. After

infiltration with 1 per cent novocain, a No. 17 intravenous needle is introduced and a groove made in the cortex of the bone, using firm pressure and a twisting motion of the needle. This needle is then withdrawn, and the Schleicher needle adjusted and pushed along the groove in the cortex at a 45° angle. It is then straightened to a right angle with the tibia, and forced down with firm constant pressure into the bone marrow cavity. When the needle passes into the marrow cavity there is a characteristic "give." When the Schleicher needle is in the marrow cavity, as confirmed by examination of its tip, a 20 cc. syringe is attached to the needle, and normal saline forced into the marrow cavity at a rate of not more than 5 cc. per minute and is again aspirated; injection and aspiration are repeated until marrow substance is found in the aspirated fluid, and the saline solution enters the cavity with relative ease. The Luer syringe with intravenous transfusion flask and tubing is then attached to the Schleicher needle, and the infusion of saline begun at a rate of 45 drops per minute for the first hour. After that period, the rate of infusion is determined by the fluid intake indicated per twenty-four hours, calculating 15 drops per minute as 1 cc. The flask is elevated at least 3 feet above the level of the needle. If the rate of flow becomes too slow, the Luer syringe may be temporarily removed, and the marrow cavity irrigated with 20 to 30 cc. of saline by repeated injection and aspiration. The Schleicher needle may be left in place for as long as seven days. This method has been found very useful for the parenteral administration of fluids to children without frequent reinsertions of the intravenous needle. Any fluid that can be given intravenously can be given by this method. The authors have never observed any signs of injury to the bone or of osteomyelitis by either clinical or x-ray examination. Three illustrative cases are reported.

Treatment of Meningococcic Meningitis in Children with a Single Intravenous Dose of Sodium Sulfadiazine

S. J. WINTER *(Journal of Pediatrics,* 26:459, May 1945) reports 9 cases of meningococcic meningitis in children treated by a single intravenous injection of a large dose of sodium sulfadiazine. The ages of the patients ranged from eight months to seven years. The dosage used was 2½ grains per pound body weight in 8 cases and 2 grains per pound in one case. The usual method employed in these cases was to begin intravenous infusion with sodium lactate 15 cc. per pound body weight; when half of this amount had been given the sodium sulfadiazine (2 to 2½ grains per pound body weight) was added to the remaining solution, the sulfadiazine being dissolved in 25 to 50 cc. distilled water. Additional sodium lactate was given later if necessary to maintain the pH of the urine or blood CO_2 at the desired level. In the cases reported it was found that this single large intravenous dose of sodium sulfadiazine maintained an adequately high level of sulfadiazine in the blood and spinal fluid for four days. In all cases spinal fluid cultures became negative in twenty-four hours; in most cases the fever subsided in twenty-four to forty-eight hours, persisting for seventy-two hours in only 2 cases. Other clinical symptoms subsided more rapidly than with the divided dose method of intravenous administration of sulfadiazine. The drug was well tolerated when adequate alkalinization of the urine was maintained. Only one of the patients showed hematuria for two days, and in this case the regular dose of sodium lactate was not given because only a limited supply was available when the patient was admitted in coma. All patients recovered without sequelae.

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Important Announcement by American Board of Ophthalmology

DUE to transportation difficulties the examination of the Board, originally scheduled for Chicago, October, 1945, has been postponed to January 18th to 22nd inclusive, 1946.

1946 Examinations: Chicago, January 18th through 22nd; Los Angeles, January 28th through Feb. 1st; New York, May or June; Chicago, October.

Medical BOOK NEWS

Edited by
ALFRED E. SHIPLEY, M.D., Dr. P.H.

All books for review and communications concerning Book News should be addressed to the Editor of this department, 1313 Bedford Avenue, Brooklyn 16, N. Y.

JOHN BOSTOCK
1733 ~ 1846

Classical Quotations

• **This state of the eyes [heat, redness, itching, smarting and a discharge of tears] comes on in paroxysms, at uncertain intervals, from about the second week in June to the middle of July. . . . ; to this succeeds irritation of the nose, producing sneezing, which occurs in fits of extreme violence, coming on at uncertain intervals. To the sneezings are added a further sensation of tightness of the chest, and a difficulty of breathing, with a general irritation of the fauces and trachea. . . . All the acute symptoms disappear about the end of July.**

JOHN BOSTOCK
***Med. Chir. Tr.* (London, 1819), x, 161-165.**

New Edition of Kolmer & Boerner

Approved Laboratory Technic. Clinical Pathological, Bacteriological, Mycological, Virological, Parasitological, Serological, Biochemical and Histological. By John A. Kolmer, M.D., and Fred Boerner, V.M.D. 4th Edition. New York, D. Appleton-Century Co., [c. 1945]. 8vo. 1,017 pages, illustrated. Cloth, $8.00.

DUE to war time directives limiting the bulk of paper this edition has been brought out in a new format which, however, compares favorably with the previous editions. There are now 30 collaborators, each an authority in his particular field. The illustrations are clear and instructive. The methods are written in a clear manner, brief and to the point with extraneous details omitted. New sections and methods have been introduced among which are methods for examination of blood and urine for hormones and vitamins. The book will be a welcome addition to the shelves of clinical pathologists, medical technologists and physicians who may have occasion to refer to laboratory methods.

DAVID M. GRAYZEL

Tissue Metabolism

Manometric Techniques and Related Methods for the Study of Tissue Metabolism. By W. W. Umbreit, R. H. Burris, and J. F. Stauffer. With Chapters on Specialized Techniques by P. P. Cohen, G. A. LePage and V. R. Potter and contributions by J. W. Bain, et al. Minneapolis, Burgess Publishing Co., [c. 1945]. 4to. 198 pages, illustrated. Fabricoid, $3.50.

THIS book is a good laboratory manual on tissue metabolism. It deals with the manometric methods of gas measurements especially oxygen and CO_2. The basis of the work is the Warburg method and its varied modifications of the measurement of oxygen uptake in cellular metabolism.

For purposes of clarification the authors define "Respiration" as the uptake of gaseous oxygen, and "Fermentation," as the transformation which occurs in living cells (or enzymes therefrom) which do not employ gaseous oxygen. A special chapter is devoted to methods of determining the value of Respiratory Quotients in metabolism.

This book is of value to all those working in the field of biology.

MORRIS ANT

Penicillin

The Story of Penicillin. By Boris Sokoloff, M.D. Chicago, Ziff-Davis Publishing Co., [c. 1945]. 8vo. 167 pages. Cloth, $2.00.

THE fascinating story of the discovery of the mold "Penicillium Notatum" by Dr. Fleming who tried unsuccessfully for years to interest the medical profession in its importance, is told by a scientist who carries the reader through the trial and error period up to the present state of our knowledge in a manner understandable by physician and laity alike.

The research work now in progress on various other antibacterial substances throughout the laboratories of the world is discussed at length.

Pages of explanatory foot notes to clarify the text and a lengthy bibliography of Penicillin and other antibiotic substances complete a short but concise review of the subject.

CHARLES G. WILLIAMSON

Circulatory Disorders

Synopsis of Diseases of the Heart and Arteries. By George R. Herrmann, M.D. Third Edition. St. Louis, The C. V. Mosby Company, [c. 1944]. 516 pages, illustrated. 12mo. Cloth, $5.00.

THE third edition of *Synopsis of Diseases of the Heart and Arteries* is a revamped and up-to-date version of its two worthy predecessors. It contains much new and valuable information and is the answer to the prayer of the practitioner who seeks knowledge in the handling of a cardiac case. Of special interest is the chapter on fluoroscopy of the heart. Essential hypertension is described as a defense mechanism on the part of the heart. and blood vessels to overcome the resistance that results from an over-stimulation of the vegetative nervous system. The chapters upon the pathologic physiology of valvular heart disease are well worth reading. Angina pectoris and coronary thrombosis are discussed in great detail and the prognosis and treatment are thorough and illuminating. Of this compact little volume it may aptly be said that the wonder grows, that one small book could carry all it knows.

SIMON FRUCHT

Pye's Surgical Procedures

Pye's Surgical Handicraft. A Manual of Surgical Manipulations, Minor Surgery, and Other Matters Connected with the Work of Surgical Dressers, House Surgeons, and Practitioners. Edited by Hamilton Bailey, F.R.C.S., Eng. 14th Edition, Revised. Baltimore, Williams & Wilkins Co., [c. 1944]. 8vo. 628 pages, illustrated. Cloth, $6.00.

THE fourteenth edition of *Pye's Surgical Handicraft* should prove to be of great value to the modern hospital house officer or general practitioner. The subject matter is very diversified, touching on the most common procedures in general surgery, as well as the specialties, that are apt to become their obligation.

The illustrations are plentiful and apt. Pre- and postoperative management of the various types of cases, anesthesias, intravenous therapy, modern chemotherapy, recognition and treatment of complications, dressings, important and pertinent laboratory determinations, the general principles in minor operations and technic, the handling of common fractures, plaster technic, and many other problems that arise in hospital work or practice are presented in an up-to-date though brief manner.

The volume is highly recommended.

WILLIAM SHEINFELD

Marihuana vs. Crime

The Marihuana Problem in the City of New York. Sociological, Medical, Psychological and Pharmacological Studies. By the Mayor's Committee on Marihuana. Lancaster, The Jaques Cattell Press, [c. 1944]. 8vo. 220 pages, illustrated. Cloth, $2.50.

UNSUBSTANTIATED reports of widespread marihuana smoking in New York City resulted in a survey under the direction of the New York Academy of Medicine at the request of Mayor La Guardia. The investigation was divided into two parts: (1) The extent of the use of marihuana, and (2) its physical and psychologic effects. No physician, psychologist or social worker can afford to miss reading this book. Some of the conclusions drawn from this study, fortunately, dispel some of the false rumors. Marihuana smoking is definitely harmful but not as bad as alleged. No direct relationship was found between crime and marihuana smoking. Also, the habit can be stopped abruptly, with no resulting mental or physical distress. These conclusions, however, should not lead the reader to believe there is no marihuana problem.

CHARLES SOLOMON

Botany of Hayfever

Hayfever Plants. Their Appearance, Distribution, Time of Flowering, and Their Role in Hayfever, with Special Reference to North America. By Roger P. Wodehouse, Ph.D. Waltham, Mass., Chronica Botanica Co., [c. 1945]. 4to. 245 pages, illustrated. Cloth, $4.75.

ALL the plants involved in the etiology of hayfever are minutely described and illustrated for the benefit of physicians and botanists, by an unquestioned authority in the science of plant life.

This volume covers the more recently developed theories regarding the role of plants in the causation of hayfever and asthma. It studies such details as season of pollination; methods of collecting and identifying these pollens; and making pollen counts. Regional surveys are included.

Discussion is made of those plants not causing allergic reactions, with the reasons for their lack of reactivity.

In our opinion this book should prove most valuable and instructive to the physician interested in hayfever. It is a "must" on the bookshelf of the allergist.

JOSEPH H. FRIES

Diseases of the Mouth

Periodontal Diseases, Diagnosis and Treatment, and Soft Tissue Lesions of the Oral Cavity. In 2 parts. By Arthur H. Merritt, D.D.S. 3rd Edition. New York, The Macmillan Co., [c. 1945]. 8vo. 256 pages, illustrated. Cloth, $3.50.

THE third edition of Dr. Arthur H. Merritt's book on Periodontal Diseases and Soft Tissue Lesions of the Oral Cavity is a vast improvement over the preceding editions. It is a ready reference work for the busy practitioner and will be especially helpful to the man in general practice of dentistry. It is well arranged and is well documented. Part One is concerned chiefly with Periodontia, Vincent's Infection, Periodontoclasia and treatment, Oral Prophylaxis, Home Care by the Patient with toothbrush technique, The Effect of Tobacco Smoking on the soft tissues of the mouth. Part Two deals with the soft tissue lesions of the oral cavity produced by avitaminosis and is particularly timely. It is a volume to be recommended to all interested in the oral cavity as a site of focal infection.

LAWRENCE J. DUNN

Robert Burton's Psychiatric Theories

The Psychiatry of Robert Burton. By Bergen Evans in consultation with George J. Mohr, M.D. New York, Columbia University Press, [c. 1944]. 8vo. 129 pages, illustrated. Cloth, $2.00.

THIS is a splendid example of close teamwork between a professor of English and a well-known psychiatrist who provide a fresh evaluation of the most popular book of its day three hundred years ago. Present-day students of psychiatry, social scientists, and philosophers, as well as the professional worker in the field of normal and abnormal psychology, will be wholesomely stimulated by the remarkably accurate observations of the one-time Oxford University professor whose book Sir william Osler called "The greatest medical treatise ever written by a layman."

The contents is composed of a sharply etched description of Robert Burton followed by a meaty digest of the latter's book which not only concerned itself with the ramification of melancholia but also various allied mental states. There follow chapters on symptomatology, etiology and therapy. Finally, the authors evaluate Burton's unique contribution in the light of modern psychiatry. A bibliography with brief comments rounds out this timely publication.

FREDERICK L. PATRY

Surgical Technique

Operations of General Surgery. By Thomas G. Orr, M.D. Philadelphia, W. B. Saunders Co., [c. 1944]. 723 pages, illustrated. 4to. Cloth, $10.00.

THE author of this volume is well known in the field of general surgery, particularly for his sound and practical teaching. In this volume he has made an excellent attempt to correlate the best of the generally accepted surgical techniques, and although the text is relatively brief, it is sufficient to explain adequately the illustrated procedures.

Various operations described are not limited to the field of general surgery, but include some of the plastic surgery, neurosurgery, urology and gynecology, which the general surgeon might at times be called upon to perform. From a teaching point of view, the brief anatomical descriptions, the indications, dangers and safeguards of the various procedures, make the volume exceptionally good for the student of surgery. The volume is orderly in its make-up, the descriptions being under the headings of the various systems.

It is to be hoped that Dr. Orr will give us more editions of this excellent book, as procedures in surgical technique and treatment improve in the future.

HERBERT T. WIKLE

Human Nature and Government

Conscience and Society. A Study of the Psychological Prerequisites of Law and Order. By Ranyard West, M.D. New York, Emerson Books, [1945]. 8vo. 261 pages. Cloth, $3.00.

IT is rare indeed to find an author so erudite in related areas of knowledge—psychoanalysis, psychiatry, psychology, philosophy, political science and legal theory—and at the same time so gifted in lucid writing. Dr. West, a practicing psychoanalyst, brings about simplification and condensation of the psychological prerequisites of government of the people. His thesis contends that laws must be based upon human nature *as it is* but as seen and synthesized with constructive convergency through the eyes of the philosopher, the lawyer, the psychologist, and the psychiatrist. Because of failure to integrate these basic knowledges and techniques, we have fallen short of our potential melioristic functioning of total human society in a total worldwide setting.

No student of human behavior can afford to overlook a critical digestion of this thought-provoking timely book.

FREDERICK L. PATRY

Female Physiology

Woman's Medical Problems. By Maxine Davis. New York, Whittelsey House, [c. 1945]. 8vo. 220 pages. Cloth, $2.00.

THIS work is a rather detailed discussion of everything from menstruation through abortion, pregnancy and their complications, sterility, cancer and the venereal diseases. It requires a fairly high degree of intelligence for its comprehension. It contains some inaccuracies and with the unqualified statement that women should "never allow a doctor to use radium," it is a little difficult to believe that it has had the careful editing by qualified medical opinion claimed for it. Most of its advice is good, other questionable.

J. THORNTON WALLACE

BOOKS RECEIVED

for review are promptly acknowledged in this column; we assume no other obligation in return for the courtesy of those sending us the same. In most cases, review notices will be promptly published shortly after acknowledgment of receipt has been made in this column.

Refraction of the Eye. By Alfred Cowan, M.D. 2nd Edition. Philadelphia, Lea & Febiger, [c. 1945]. 8vo. 278 pages, illustrated. Cloth, $4.75.

Your Hair and Its Care. By Oscar L. Levin, M.D. & Howard T. Behrman, M.D. New York, Emerson Books, [c. 1945]. 12mo. 184 pages, illustrated. Cloth, $2.00.

Manual of Prescription Writing and Medical Jurisprudence. By Harold N. Wright, Ph.D. 2nd Edition. Minneapolis, Burgess Publishing Co., [c. 1944]. 4to. 117 pages, illustrated. Fabricoid, $1.50.

Studies in Biophysics: The Critical Temperature of Serum (56°). By Lecomte Du Noüy, D.Sc. New York, Reinhold Pub. Corp., [c. 1945]. 8vo. 185 pages, illustrated. Cloth, $3.50.

Hidden Hunger. By Icie G. Macy, Ph.D. & Harold H. Williams, Ph.D. Lancaster, Pa., The Jaques Cattell Press, [c. 1945]. 8vo. 286 pages, illustrated. Cloth, $3.00.

The Care of the Neurosurgical Patient. Before, During and After Operation. By Ernest Sachs, M.D. St. Louis, C. V. Mosby Co., [c. 1945]. 8vo. 268 pages, illustrated. Cloth, $6.00.

Clinical Biochemistry. By Abraham Cantarow, M.D. & Max Trumper, Ph.D. 3rd Edition. Philadelphia, W. B. Saunders Co., [c. 1945]. 8vo. 647 pages, illustrated. Cloth, $6.50.

Facial Prosthesis. By Arthur H. Bulbulian, D.D.S. Philadelphia, W. B. Saunders Co., [c. 1945]. 8vo. 241 pages, illustrated. Cloth, $5.00.

Bacillary Dysentery, Colitis and Enteritis. By Joseph Felsen, M.D. Philadelphia, W. B. Saunders Co., [c. 1945]. 12mo. 618 pages, illustrated. Cloth, $6.00.

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PULMONARY TUBERCULOSIS

—Continued from page 287

creased shadows at the left hilus. The plate taken about a year later on July 20, 1940, after the lung was allowed to reexpand almost completely, shows only a residual increase in surface markings and no evidence of any tuberculous process.

Except for two weeks' hospitalization, this patient remained at home and received pneumothorax refills at the doctor's office at stated intervals. Exactly six weeks after the initial pneumothorax treatment, he was able to return to his former occupation, that of public accountant. This man has been examined recently and shows no clinical or fluoroscopic evidence of the previous lesion.

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(To be continued)

EDITORIALS

—Concluded from page 282

Significant of the "common man's" amenability to war and its evils is the exploitation by press and movies of the fascination and thrill which he gets from gruesomely detailed atrocities.

The physician, *artist in the salvage of life*, cannot happily adjust to either form of murder.

CANCER

—Concluded from page 299

6. Cutler, M., Buschke, J. F. and Cantril, S. T. *Cancer, Its Diagnosis and Treatment.* Philadelphia, Saunders, 1938, p. 212.
7. *Ibid.*, pp. 200 and 203.
8. *Sci. News Letter*, May 2, 1942, p. 277.
9. Hoffman, F. L., cited by Dingman (3), p. 83.

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